Annual Meeting • Chicago • June 11-15, 1956

DOES NOT CIRCULATE

This Issue Exceeds 160,000 Copies

THE JOURNAL

OF THE

American Medical Association

UNIVERSITY OF MICHIGAN

APR 3 1956

MEDICAL LIBRARY

MARCH 31, 1956

ORIGINAL ARTICLES

TREATMENT OF THROMBOEMBOLISM 1101
J. H. Olwin, M.D., Chicago
BILATERAL AND RECURRENT RENAL CALCULI 1106
Roger Baker, M.D., and J. P. Connelly, M.D., Washington, D. C.
COMPLETE NUTRIMENT FOR THE THERAPY OF PEPTIC ULCER 1111
Asher Winkelstein, M.D., and Eric Schweiger, M.D., New York
PROGRESS IN PREVENTION OF CHRONIC ILLNESS, 1949-1956 1114
L. A. Scheele, M.D., Washington, D. C.
PERSISTENCE OF ABNORMAL HEPATIC TESTS IN CARRIERS OF VIRAL HEPATITIS 1118
R. F. Norris, M.D., Dicran Kassouny, M.D., J. G. Reinhold, Ph.D., and J. R. Neefe, M.D., Philadelphia
AGED IN CONNECTICUT STATE MENTAL HOSPITALS 1121
Sidney Shindell, M.D., and Elizabeth Cornfield, M.D., Rocky Hill, Conn.
INTERMITTENT POSITIVE-PRESSURE BREATHING 1125
Alan Leslie, M.D., D. A. Dantes, M.D., and Leon Rosove, M.D., Los Angeles

CLINICAL NOTES

NITROGEN MUSTARD IN TREATMENT OF ADVANCED CARCINOMA OF LUNG 1129
H. B. Hatch, M.D., J. K. Bradford, M.D., and Alton Ochsner, M.D., New Orleans
SERUM GLUTAMIC OXALACETIC AMINOPHERASE (TRANSAMINASE) IN HEPATITIS 1130
Felix Wróblewski, M.D., and J. S. LaDue, M.D., Ph.D., New York
THE L. E. CELL AS A MANIFESTATION OF DELAYED HYDRALAZINE INTOXICATION 1134
Phillip Comens, M.D., and H. A. Schroeder, M.D., St. Louis
IMPROVED NONCRUSHING CLAMP FOR USE IN GASTROENTEROLOGICAL OPERATIONS 1136
W. F. Rienhoff, M.D., Baltimore

SPECIAL ARTICLE

HARVEY AND MEDICAL RESEARCH 1137
L. N. Katz, M.D., Chicago

SPECIAL REPORTS

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES 1142

EDITORIALS

Potential Values of the Autopsy Today ..1144
Isaac Starr, M.D.
Commission on Chronic Illness 1145

THE PRESIDENT'S PAGE

A Monthly Message 1146

ORGANIZATION SECTION

Investment Advisor for A. M. A. 1147
Advisory Committee on Television and Motion Pictures 1147
A. M. A. Grants-in-Aid for Research ... 1147
Appointment of New Editor 1147
Network Television Shows 1147

REGULAR DEPARTMENTS

Medical News 1148
Meetings 1152
Examinations and Licensure 1155
Magazine-Television Report 1155
Government Services 1156
Deaths 1157

Foreign Letters:
Austria: Thrombopenia with Aplasia of Radius. Neonatal Metabolism and Renal Function. Terebrating Carcinoma. Roentgenography of the Bile Passages 1161
Brazil: Gas Gangrene. Dr. Adolfo Lutz's Centennial. Ascariasis 1161
Colombia: Cancer. Centers of Public Assistance 1162
Denmark: Ornithosis. Morphine Poisoning. School for Medical Secretaries. 1162
France: Hormonal Treatment of Tuberculosis. Diverticulosis of the Small Intestine. Operation in Lung Abscess. Malignant Cardiac Rheumatism. Psychic Disturbances and Osteitis Deformans of Skull. Methyl Bromide Poisoning. Tonsillectomy and Inflammatory Rheumatism. Surgeon's Responsibility. Dietary Deficiency and Recourse to Alcohol. Local Hyperemiants in Arteritis ... 1162
India: Vaginal Carcinoma. Carcinoma of the Breast. New Local Anesthetic. Amebic Infections 1163
Italy: Congress of Industrial Medicine. Psychological Tests and Myopathies. 1164
Peru: Nonfunctioning Tumors of the Adrenal Gland. Social Welfare and the Medical Association 1164
Sweden: Medical Certificates for Policemen 1165
Switzerland: Diabetes. Neurosurgery. Aldosteronuria and Hyperkalemia .. 1165
United Kingdom: Long-Term Chemotherapy in Pulmonary Tuberculosis. Copper in Food. Sleep Behavior in the Aged. Emergency Bed Service. Prescribing Drug Samples. What Is a Drug? Poliomyelitis and Smallpox Vaccination. Cadmium Poisoning and Byssinosis. Orally Given Poliomyelitis Vaccine 1166
Correspondence:
Drugs for Arthritis. Transfusion Service in Atomic Bombardment Areas 1168
Medicolegal Abstracts 1170
Miscellany:
The Doctor Looks at the Cancer Program 1171
Medical Literature Abstracts 1173
Book Reviews 1181
Queries and Minor Notes:
Prevention of Tuberculosis Among Student Nurses. Hypotension. Infections Due to Mima Organisms. Crossed Cylinder in Refraction. Large Fat Deposits on Legs. Fibrocystic Disease of Pancreas. Toilet Rooms. Flight After Pneumonectomy. Priapism and Antihistamines. Acne. Rehabilitation. Pain over Gallbladder Following Accident. Cecotomy. Fitting Shoes with X-Ray Machines. Endometriosis of the Pleura. Headache in Young Girl. Removal of Calculus in Parotid Duct. Tetanus Immunization. Parasites in Pigeons. Eczema at Onset of Menstruation ... 1183

WASHINGTON NEWS

Insurance for U. S. Employees. Osteopaths in Military Service. Armed Forces Medical Library. Opposition to Disability Section. Salk Vaccine. Adv. Page 11
From Other Pages ..... Adv. Page 40
National Organizations of Medical Interest ..... Adv. Page 45
Tonics and Sedatives ..... Adv. Page 60
The Bright Side ..... Adv. Page 76
Index to Advertisers ..... Adv. Page 85

Volume 160, No. 13 Published Weekly at 535 North Dearborn Street, Chicago 10, Illinois. Subscription, $15. Single Copy, 45 cents

New (2nd) Edition—**Wolff's Electrocardiography**

A wonderfully useful book bringing you new understanding of the electrocardiogram—largely eliminating need for memorization of patterns. Includes new material on the arrhythmias and vectorcardiography.

See SAUNDERS Advertisement on next 2 pages

UNIV OF MICHIGAN GENERAL LIBRARY ANN ARBOR MICH

A4B084704/CS 126

New (2nd) Edition

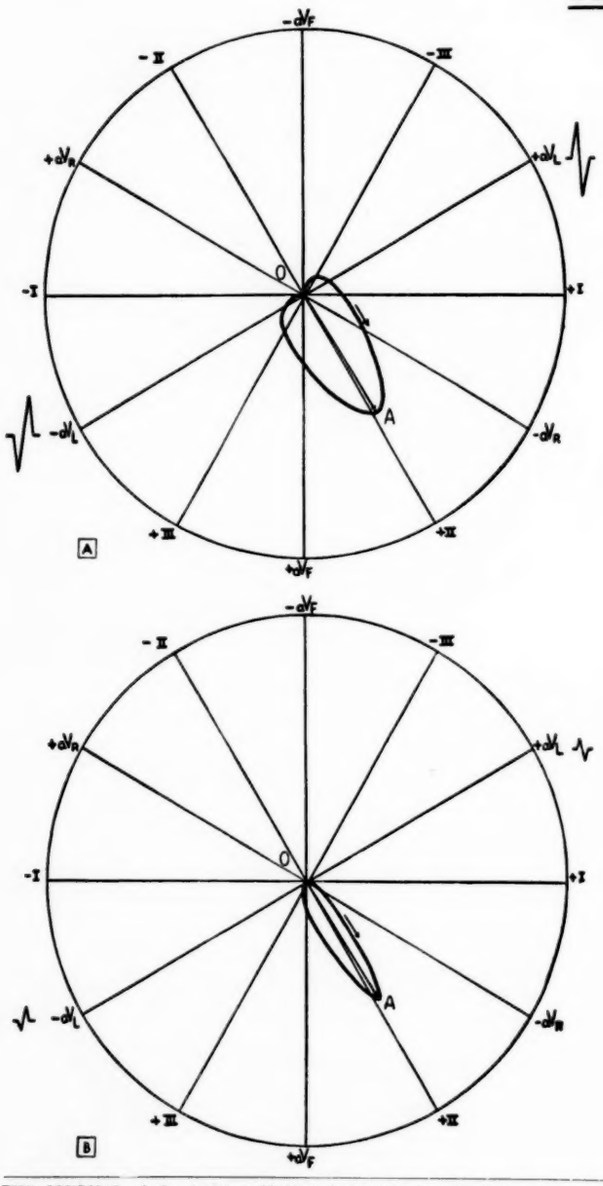
Explains the electrocardiogram so you can readily understand and evaluate any tracing—without remembering patterns

WOLFF'S

Figure 56. A normal frontal plane vectorcardiogram. It is a smooth elliptical figure without sharp or sudden indentations. All the instantaneous vectors are grouped symmetrically about the maximum vector. OA, which corresponds to the mean vector in Figure 55, or its projection on the lead II axis, RII, in Figure 54. The projection of these vectors onto a lead axis perpendicular to the maximum vector, i. e., on lead aV_L, will yield R and S waves of equal amplitude. Lead aV_L represents the transitional zone, and the equal R and S deflections the transitional complex. The magnitude of the R and S deflections in the transitional complex will depend on the width of the QRS loop. See text.

A, wide loop, and large transitional complexes.

B, narrow loop, and small transitional complexes.



CONTENTS

PART I—Electrical Phenomena & Muscle Contraction. Electrical Properties of Cell Membrane. Depolarization. Dipoles. 3

Volume Conductors. Unipolar and Bipolar Leads 8

Deflections Which Represent Depolarization. Intrinsic and Intrinsicoid Deflections 18

Vector Representation of Dipoles. Vector Summation. Anatomy and Physiology of the Heart 25

The Electrical Effects of the Simultaneous Excitation of Two Muscle Masses in a Volume Conductor 30

The Electrical Field Around the Heart 35

Repolarization. Primary and Secondary T Wave Changes 41

The Precordial Electrocardiogram 47

Unipolar Limb Leads. Standard Limb Leads 52

The Einthoven Equilateral Triangle Hypothesis. Instantaneous and Mean Electrical Axis. Ventricular Gradient 58

Right and Left Bundle Branch Block 71

Left and Right Ventricular Hypertrophy 80

The Effect of Muscle Injury on the Electrocardiogram 90

Current of Injury. Blocking of the Depolarization Wave 96

Myocardial Infarction 101

PART II—Introduction: Normal and Abnormal Electrocardiograms. Instruments. Technique. Nomenclature 111

The Normal Electrocardiogram 119

Bundle Branch Block 143

Left and Right Ventricular Hypertrophy 166

Coronary Heart Disease. Myocardial Infarction 193

Myocardial Infarction and Bundle Branch Block. Infarction of the Interventricular Septum. Persistent S-T Segment Displacement. Aborization Block 222

Pericarditis. Pulmonary Embolism. Abnormal Electrolyte Patterns 236

Short P-R Interval with Abnormal QRS Complexes 250

PART III—The Cardiac Mechanism 267

Normal and Abnormal S-A Nodal Mechanisms 272

Ectopic Arrhythmias: Atrial & Ventricular Premature Beats; Paroxysmal Atrial and Ventricular Tachycardia 279

Atrial Flutter and Fibrillation 302

Etiology of Paroxysmal Rapid Heart Action 312

A-V Nodal Rhythm. A-V Dissociation. Parasystole. Carotid Sinus Stimulation 314

Atrioventricular Block 322

THE JOURNAL of the American Medical Association is published weekly by the American Medical Association. Subscription price, $15.00 a year, 45c a copy. Canadian $17.00. Foreign $21.50. Entered as second class matter June 25, 1885, at the Postoffice at Chicago, Ill., under act of March 3, 1879. Address all communications to American Medical Association, 535 N. Dearborn St., Chicago 10, Illinois

THE JOURNAL
of the American Medical Association
Published Under the Auspices of the Board of Trustees
VOL. 160, NO. 13 CHICAGO, ILLINOIS MARCH 31, 1956
COPYRIGHT, 1956, BY AMERICAN MEDICAL ASSOCIATION

TREATMENT OF THROMBOEMBOLISM

John H. Olwin, M.D., Chicago

• *The treatment of thromboembolism has been changed by the development of antibiotics and anticoagulants. The rationale of phlebotomy to remove thrombi and of ligation of large veins to prevent embolism is now questioned, since further surgery increases the circulatory difficulties and dangers. Ligation for thromboembolism is indicated only when anticoagulants are contraindicated or when embolism recurs in spite of them.*

Unchanged, however, are certain other principles of treatment. If the healing processes cannot be aided, they must at least not be hindered. Warmth is valuable, but overheating must be avoided. It is particularly important to make sure that the arterial supply to the part is adequate, for the increased metabolic demands of warmed extremities will cause serious damage to tissues with inadequate blood supply.

These principles apply generally to superficial and deep thrombophlebitis, to acute subclavian thrombosis, migratory thrombophlebitis, subacute and chronic thrombophlebitis, peripheral embolism, and the postphlebitic syndrome. Anticoagulants have reduced the danger of pulmonary embolism and have improved the prospects of the patient with thrombosis of the central retinal artery. In mesenteric thrombosis, heparin is given as soon as the diagnosis is made, for the anticoagulant does not cause unusual bleeding during the necessary resection of the affected intestinal segment.

The voluminous literature and the diversity of opinion as to the cause and treatment of thromboembolism are testimony to the complexity of the problem. There is little real knowledge as to its cause, and only in recent years have any advances been made in the methods of its treatment. Out of the great amount of work that has been done in the field, and in a large part quite by chance, the treatment of the various aspects of thromboembolism has advanced materially during the last decade. It is the purpose of this paper to present some of the methods of treatment and to offer personal criticism of them.

General Considerations

Certain age-old principles are still of primary importance in the treatment of thromboembolism. Of these, rest is still the most important form of therapy. Since most thrombi occur in the lower extremities, immobilization of the patient is mandatory and must be insisted upon until the signs and symptoms have disappeared almost completely. The demands of function inhibit, for the most part, the healing processes, and these, if they cannot be aided, must not be hindered. Next in importance to rest is elevation of the part. This is particularly true in involvement of the lower extremities, where the return circulation is poor at best and in the pathological state is poorer still. The early disappearance of swelling is important in the return of the limb to normal, for the longer swelling persists the more permanent become the trophic changes in the skin and subcutaneous tissues and to a certain extent in the deeper structures. Elevation must be continued until the part, as indicated by inspection and palpation, has returned to normal.

Since most of the antiphlogistic and various healing processes are aided by an increased circulation, heat is, as a rule, a desirable adjunct. Blanket packs encasing the whole part and covered with a heat cradle or electric pads should be applied as early as possible. Care should be exercised to avoid burning, and it is particularly important to ascertain that the arterial supply to the part is adequate. The increased metabolic demands of warmed extremities may cause serious damage to tissues with inadequate arterial supply. This, of course, is extremely important in elderly patients, but some persons even in their 20's have an extreme degree of atherosclerosis, and all extremities should be carefully examined before heat is applied.

Heat is often a welcome factor in the relief of pain. Vasospasm is probably one of the primary causes of pain, and heat will be a factor in neutralizing it. The use of sympathetic ganglion block for this purpose has in recent years obtained considerable favor and often brings immediate relief of pain. Whether it is of benefit beyond this one effect is still a matter of conjecture, but certainly its use has few contraindications and may be of real benefit.

From the Department of Surgery, the Presbyterian Hospital, affiliated with the College of Medicine, University of Illinois.

The infection factor in thromboembolism varies to a wide degree but is important in certain types of the disease. Where fever is present, antibiotics should be used and the individual drug should be adapted to the patient's tolerance. Its use may be discontinued when the temperature returns to normal.

During the early years of World War II thrombophlebitis was often treated by phlebotomy, removal of the thrombus or part of it by aspiration, and ligation of the vein. Early in the postwar period ligation alone was done for the prevention of emboli. In certain centers routine bilateral superficial femoral ligation was done prophylactically in all elderly patients undergoing major surgery. The rationale of these procedures warrants examination. In a patient with a demonstrated tendency toward intravascular clotting, further surgery must add more thromboplastic substances to the blood stream as well as further trauma to blood vessels and surrounding tissues—two factors that, in the light of our present knowledge, may play etiological roles in thromboembolism. In addition, if the principle of ligation to prevent embolism is carried to its logical conclusion, the great veins should be ligated at the heart, since emboli may and do form above the points of ligature. If the collateral circulation about these points is adequate, postligation edema does not follow, but, when iliofemoral or femoral thrombophlebitis is severe, collateral veins may be extensively involved and permanent edema follow ligation. Many patients have become permanent invalids after ligation of the vena cava.

It is my opinion that ligation for thromboembolism is rarely indicated and in our present state of knowledge should be used only when anticoagulants are contraindicated or in the rare instances where embolism recurs in spite of them. Anticoagulants have become an accepted and important part of the treatment of most thromboembolic conditions. In most patients their judicious use is safe and effective in the limitation of the clotting process and the prevention of embolism. When administration of anticoagulants is started early in the disease and continued the proper length of time along with rest, elevation of the part, supportive dressings, and, where indicated, antibiotics, the average patient with thrombophlebitis may expect to recover completely. The detailed management of anticoagulant therapy has been covered elsewhere [1] and is beyond the scope of this paper.

If there has been swelling of the leg to any degree during the acute phase, and if it has persisted for more than a few days, constrictive stockings and/or bandages must be applied when the patient gets out of bed and their use continued until the physician is assured that edema will not recur.

Superficial Thrombophlebitis

The most common form of superficial thrombophlebitis is that occurring in varicose veins. There may be single or multiple sites of inflammation, with the secondary sites occurring simultaneously with or subsequent to the original. Heat, rest, elevation, and antibiotics will usually result in an early resolution of the condition. Six weeks after the onset, if there have been no new sites of inflammation, the saphenous system or systems involved should be surgically removed by ligation and stripping of the main channels and excision and/or stripping of all the palpable tributaries. Many of these patients will do well without anticoagulants, but, because of recurring episodes prior to surgery in some and an occasional involvement of the deep veins (a rare complication), it is worthwhile to institute a short course (two to three weeks) of anticoagulant therapy.

Superficial thrombophlebitis not infrequently occurs in veins being used for intravenous infusions. The needle or catheter should, of course, be removed from the vein and rest, heat, elevation, and antibiotic therapy started. In the young this treatment may be adequate; however, many patients with this condition are elderly and somewhat debilitated, and, with the added factor of surgery, extension to the deep veins is not infrequent. Local clinical signs of extension to the deep veins may be lacking, and the earliest evidence may be a pulmonary embolus; anticoagulant therapy should therefore be instituted and continued for a minimum of three weeks.

Recurrent superficial thrombophlebitis with or without varicose veins, particularly in the male under 35, may be the first sign of thromboangiitis obliterans (Buerger's disease). None of the usual forms of therapy for thrombophlebitis, including excision of the veins and anticoagulants, will be effective in such cases; however, the interdiction of the use of tobacco may be sufficient to prevent recurrence.

Femoral or Iliofemoral Thrombophlebitis

Clinicians today are prone to think of femoral and iliofemoral thrombophlebitis as occurring in two forms: the full-blown thrombophlebitis of the extremity, with swelling, redness, tenderness, fever, and often a chill, as compared to the less dramatic so-called phlebothrombosis, which may go completely unnoticed or which may manifest itself by a slight rise in the pulse rate, a slight fever, and a mild tenderness over the calf and/or femoral vessels. Homans' sign may or may not be present. Phlebothrombosis will frequently first manifest itself clinically by a pulmonary embolus, and even after such occurs it may be impossible to determine its site of origin. The first condition is treated with the usual rest, elevation, blanket packs from toes to groin if the iliac vessels are involved, and with antibiotics. Anticoagulant therapy is started early, heparin being used initially and its use being discontinued only after the prothrombin has been reduced to a therapeutic level with one of the prothrombin depressants. Antibiotic therapy is discontinued after the patient becomes afebrile, and the elevation of the limb is continued until swelling has completely disappeared. Because of the maceration of the skin with continuous warm moist dressings, these may be alternated at six-hour intervals after the first two or three days. As soon as the swelling has disappeared, the patient may be ambulant for brief periods with the support of an elastic stocking or bandage: in some instances both will be necessary in order to prevent a return of the swelling. It should be emphasized that the swelling must not return if the patient is to have a normal limb, and whether the achievement of this status requires three weeks, three months, or six months, there can be no compromise.

The anticoagulant therapy should be continued with the patient on an ambulant, outpatient basis for at least a month after all signs of swelling and induration of the soft tissues of the leg have disappeared, and the restrictive stocking and bandages should be used until their use can be gradually discontinued without return of even a minimal amount of swelling. Under this routine there will be few limbs that will not return to normal appearance and function.

Cases of phlebothrombosis should have similar treatment, but it may be unnecessary to use antibiotics, particularly if there is no fever. If the signs and symptoms disappear after a few days of therapy, as they frequently do, the patient may be allowed out of bed provided his condition is controlled with anticoagulants. Therapy with anticoagulants is continued usually for a minimum of three weeks. Constrictive stockings or bandages may be unnecessary, particularly if there is no edema with ambulation. It is wise to see that the condition of such patients is completely controlled with anticoagulants as soon as the diagnosis is made or suspected.

Acute Subclavian Thrombosis

Thrombosis of the subclavian vein is a condition occurring most often in young adult males who are actively engaged in sports or vigorous types of work. Trauma is likely an important factor in this condition. The early treatment consists of elevation, blanket packs, and anticoagulant therapy. Antibiotics are used if the patient has fever. Since it is more difficult to maintain continuous elevation of the arm than of the leg, the resolution of this condition is prolonged. Anticoagulant therapy should be continued for a minimum of six weeks, and if it is at all possible the patient should be immobilized and the arm elevated continuously. Most patients will object to this and as a result may go for months and even years with a swollen arm. The condition is less prone to recur than thrombophlebitis of the leg, but recurrent episodes are best taken seriously and the patient immobilized until all signs and symptoms have disappeared.

Migratory Thrombophlebitis

Migratory thrombophlebitis is a condition in which venous thrombosis occurs at different sites, usually in one leg or the other in rapid succession; however, the attacks may be separated by intervals during which the patient is free from signs and symptoms. It may be present in young adults, or the first attack may appear in later adult life. Attacks may be days or years apart. The treatment of single episodes is the same as described in the discussion of iliofemoral thrombophlebitis, except that patients who have had several episodes in a relatively short time should have continuous anticoagulant therapy. Patients with attacks at intervals of several years should not be given continuous anticoagulant therapy. Such therapy is, of course, inconvenient and expensive. It is, however, less expensive than the treatment of recurring attacks at frequent intervals, and the fact that persons can carry on their usual work while undergoing treatment makes continuous anticoagulant therapy a welcome alternative. It is worthwhile for a patient with migratory thrombophlebitis who has been receiving anticoagulant therapy for a period of two years to have a trial without such therapy. Some of these patients may go along indefinitely without recurrence, but less fortunate ones must again be given continuous anticoagulant therapy for another two or three years before they can be given another trial without anticoagulants. Patients with migratory thrombophlebitis should be carefully screened for the possibility of disease elsewhere, particularly tumors or inflammation of the pancreas, for, while anticoagulants will control most cases of recurring thrombophlebitis, they are often ineffective against conditions complicated by pancreatic abnormalities.

Subacute and Chronic Thrombophlebitis

There are patients who walk about for months after episodes of thrombophlebitis of a low grade. They may have a mild swelling of the leg with tenderness and induration of the calf and other muscles, but they are unwilling to undergo adequate therapy or for other reasons have not received it. They must be placed on a regimen of bed rest with elevation of the limb, and anticoagulant therapy must be started. This routine must be maintained until all signs of abnormality have disappeared, when the patients can be ambulated with proper constrictive stockings or bandages. The slightest recurrence of induration or swelling is reason to return such patients to bed rest and elevation. Anticoagulant therapy should be continued for a minimum of three months after all signs and symptoms have disappeared. Provided that the condition has not caused extensive fibrous tissue formation in the subcutaneous and other soft parts of the limb, patients receiving such a routine may expect eventually to have normal extremities.

Postphlebitic Syndrome

The patient who has had inadequately treated single or recurring episodes of thrombophlebitis of the leg eventually finds himself with a limb that is chronically swollen, painful, discolored, and, after a period of time, extensively ulcerated. The deep veins of such legs are usually dilated, the walls thickened, and the valves completely incompetent. The soft parts are permanently altered, and there may be extensive secondary varicosities. These limbs cannot be returned to normal by any form of treatment, but the patient can be materially aided and, over a period of time, the limb restored to a reasonably normal function. The patient must first be placed on a regimen of bed rest, with the limb elevated, and ulceration, if it exists, must be healed. The skin about the ulcer may frequently be infected with a variety of organisms. The ulcer should be bathed gently each day with mild white soap and water, and, if the arterial circulation is not impaired, 3% salicylic acid in tincture of merthiolate should be applied following such cleansing. Most ulcers will respond early to such treatment. Varicosities should be ligated and/or stripped after the areas of ulceration have been healed. In some instances in which perforating veins are present immediately below the ulcer the veins can be taken out only by a complete excision of the ulcer bed and the application of a split-thickness skin graft. When the maximum reduction of swelling has occurred and when no further diminution can be achieved, the patient can be allowed out of bed with a supportive stocking and elastic bandage, the latter extending from

the base of the toes to the knee. He should be urged to elevate his leg at every possible opportunity for the remainder of his life. Ligation of the deep veins should be limited to those patients in whom there is a rapid swelling of the limb and a feeling of bursting pain on assumption of an upright position. I have found popliteal ligation to be as satisfactory as femoral.

Some patients with the postphlebitic syndrome are unable to follow the foregoing program for economic reasons. These patients can be benefited a great deal if the routine of soap and water hygiene, fungicides, and constrictive dressings is instituted on an ambulatory basis. The only variation is that after one layer of absorbent gauze impregnated with petrolatum is placed over the areas of ulceration, sterile gauze is placed about the leg and a single layer of 0.25 in. foam rubber is wrapped about the entire lower leg. This is bound into position with a 4 in. tensor elastic bandage, and the patient is urged to elevate his leg at every possible moment out of each 24 hours. The bandage and dressings are removed at night, the patient washes the ulcer and skin with mild white soap and water, the 3% salicylic acid in tincture of merthiolate is applied, and the limb is left completely uncovered until morning.

Patients with the postphlebitic syndrome are frequently treated to a point beyond which no improvement is apparent. On the supposition that a low-grade chronic thrombophlebitis exists in most of these cases, anticoagulant therapy is then instituted. The greater number of these patients receive further benefit subjectively and objectively from this additional therapy. As a result I now add this form of therapy to the beginning routine. It is usually continued for from three to six months and in some instances for a somewhat longer period of time. These patients must realize that they will never have normal legs but that with proper care they will be able to carry on relatively normal lives with a useful limb.

Central Retinal Vein Thrombosis

Until recent years the ophthalmologist had little to offer the patient with retinal vein thrombosis. This condition sometimes undergoes resolution, but more often it progresses, resulting in glaucoma and loss of the eye. It is one of the more satisfactory types of thrombosis from the point of view of the influence of anticoagulants. When seen and treated early, patients with this condition may anticipate improvement and many of them experience a return of normal vision. Results are less gratifying when therapy is not started until three to six weeks after onset of the condition, but some patients will show improvement even after such a delay. The entire routine may be carried out on an outpatient basis, and therapy is continued as long as the eye shows progress. Recurrence is not infrequent and indicates the need for continuous anticoagulant therapy. In my experience, one patient with bilateral central retinal vein thrombosis has been receiving such therapy for more than seven years without recurrence.

Pulmonary Embolism

The chief objective in the treatment of pulmonary embolism is its prevention. Once it occurs in the nonfatal form certain complications such as pleural effusion and pneumonia will require active therapy, but the primary concern in this condition is its prophylactic treatment. About one-third of the fatal pulmonary emboli are preceded by nonfatal ones. When one occurs or is suspected, anticoagulant therapy should be initiated without delay. Blood is withdrawn for determination of prothrombin and coagulation time, and 50 mg. of heparin is given through the same needle. Absolute control of the patient's condition must be maintained with heparin until the prothrombin has been reduced to therapeutic levels with a suitable prothrombin depressant. The use of both the one-stage and two-stage prothrombin methods provides for greater uniformity and safety in anticoagulant control than use of only the one-stage method. The patient is placed on a regimen of bed rest, disturbed as little as possible, and enemas interdicted. He is allowed up in a chair after five days providing his anticoagulant therapy is continued and any signs of phlebothrombosis have disappeared. These latter, of course, may never have been present. Anticoagulant therapy is continued for a minimum of six weeks, with the patient going home two weeks after the embolism has occurred if his condition otherwise permits.

I have seen no fatal emboli when the above routine has been followed. An occasional nonfatal one has followed the institution of therapy. These are considered to be loosely adherent thrombi that were ready to break off at the time therapy was started, and, of course, they were not prevented from doing so by anticoagulants. Ligation is reserved for the rare patient in whom anticoagulants are contraindicated and who has had one major embolism or repeated smaller emboli and for the still rarer patient who, despite controlled anticoagulant therapy, continues to have emboli.

Mesenteric Thrombosis

Once the diagnosis of mesenteric thrombosis or embolism has been made, celiotomy and resection of the involved intestine are indicated, except in most unusual circumstances. Heparin is given intravenously as soon as the condition is apparent and its administration continued postoperatively along with prothrombin depressants. When the therapy is carefully controlled, such patients are in little danger of hemorrhage, extension of the clot being the chief hazard prior to and after surgery. Heparin given intravenously in therapeutic doses immediately prior to surgery does not result in unusual bleeding during the operation.

Peripheral Embolism Problem

The young adult with rheumatic heart disease and auricular fibrillation and the usually older patient with myocardial infarction may be subject to recurrent emboli lodging in the extremities, brain, abdominal organs, and, when the right side of the heart is involved, the lungs. The treatment is directed toward (1) the restoration of the circulation to the part by (*a*) removal of the block when possible and/or (*b*) increasing the collateral circulation and (2) prevention of further embolism. Emboli lodging in the legs at the popliteal bifurcation and above will usually require surgical removal at the earliest possible moment after their occurrence. The same is true of

those lodging in the arteries of the arm and shoulder at and proximal to the origin of the deep brachial branch.

In patients in whom emboli occur in small vessels distal to the popliteal and deep brachial, sympathetic ganglion block should be carried out and anticoagulant therapy started 20 minutes later. The block should not be repeated after anticoagulant therapy has been started because of the danger of severe and possibly fatal hemorrhage. Sympathetic ganglion block may be used early in emboli lodging higher, but, since it must delay the institution of anticoagulant therapy, it is not used routinely. An alternative to its routine use is the employment of spinal anesthesia. Once the diagnosis is made the patient is rapidly transferred to surgery, a spinal anesthetic administered, and heparin given 10 minutes later. Embolectomy may then be carried out. If a peripheral pulse returns, surgery is unnecessary. Return of color and heat without return of pulse is not sufficient improvement, particularly in the younger patient, to obviate the need for embolectomy.

After surgery, the adjusted dose of heparin is repeated every four hours until the prothrombin is controlled by a prothrombin depressant. The extremity is protected from trauma and kept in a neutral position, or an oscillating bed may be used at intervals, if one is available. I have used the positive-negative pressure glass boot on occasions and have felt it may have aided in relieving vasospasm and increasing collateral circulation.

Unless there is definite contraindication, all patients with rheumatic heart disease and auricular fibrillation who cannot be converted to regular rhythm are candidates for continuous anticoagulant therapy. Such therapy, if properly controlled, is effective in preventing embolism in most patients.

The difficulty in distinguishing between cerebral embolus, thrombosis, and hemorrhage is often responsible for the policy of watchful waiting in the treatment of cerebral accidents—a policy that is in most instances above criticism. When cerebral embolus is reasonably certain, sympathetic ganglion block may be carried out, followed by anticoagulant therapy.

Prophylactic Use of Anticoagulants

The use of anticoagulants in the prevention of thrombosis and embolism has been discussed under various paragraphs throughout this paper. There is, however, a broad field of prophylaxis in patients who have had a history of thromboembolism and who expect to undergo surgery and/or expect for one reason or another to be confined to bed for an extended period of time. This may apply to medical patients as well as surgical, since a high percentage of thrombosis and embolism is observed in medical patients. Varying with the judgment of the physician or surgeon, these patients are considered proper candidates for anticoagulant therapy in the immediate postoperative periods and during any period in which they necessarily may be confined to bed.

Summary and Conclusions

The age-old practices of rest and elevation of the part in the patient with thrombophlebitis are still the most important factors in the treatment of this condition. The relief of vasospasm by heat and sympathetic ganglion block are valuable aids in the therapy, the heat being of additional aid in increasing the metabolism of the affected part. The use of heat is contraindicated in the presence of arterial insufficiency. Antibiotics are recommended when fever is present. Anticoagulants are an important addition to the therapy of thromboembolism and will in most instances limit the clotting process and prevent embolism from either peripheral veins or heart. Ligation of veins should be done only when anticoagulants are contraindicated or when embolism recurs despite anticoagulant therapy, a rare occurrence when the latter is adequately controlled.

Constrictive stockings and/or bandages are important in controlling edema in the postphlebitic period and must be worn as long as perceptible swelling persists. Peripheral emboli lodging at or proximal to the origin of the deep brachial artery and popliteal bifurcation should as a rule be removed surgically, while serious effects of those occurring below these levels will usually be prevented by the use of sympathetic ganglion blocks and anticoagulants. Continuous long-term anticoagulant therapy is a safe procedure and will in most instances prevent the recurrence of thrombophlebitis and embolism. Patients with the postphlebitic syndrome will seldom be cured but may be restored to a comfortable useful life by means of rest, elevation of the part, antibiotics, anticoagulants, constrictive dressings, and sometimes skin grafting and popliteal vein ligation.

30 N. Michigan Ave. (2).

1. Olwin, J. H.: The Control of Dicumarol Therapy, Am. J. Med. Sc. **217**: 427-437 (April) 1949. Pascale, L. R., and Olwin, J. H.: Clinical Experience with a New Anticoagulant, Dipaxin (2-diphenyl-acetyl-1,3-indandione), Circulation **9**: 230-237 (Feb.) 1954. Olwin, J. H., and Friedman, I. A.: The Control of Tromexan Therapy, Surg. Gynec. & Obst. **99**: 22-28 (July) 1954. Olwin, J. H.: Methods for Prothrombin Assay: Theoretical and Practical Considerations, Schweiz. med. Wchnschr. **29**: 817-820 (July) 1954; Symposium on Clinical Advances in Medicine: Principles of Anticoagulant Therapy and Their Application, M. Clin. North America **39**: 227-240 (Jan.) 1955.

The Psyche in Allergic Disease.—In order to be a good allergist, it is necessary to be equipped with something more than just bottles of extract and syringes. That something is the ability to blend allergic therapy and psychotherapy to meet the needs of the patient. The physician must first evaluate the physical and psychologic factors in each individual case. Where physical factors predominate, the allergist can do the greatest good for his patient by applying sound principles of allergic investigation and therapy, in addition to establishing a doctor-patient relationship which will encourage the patient to speak of his emotional problems. Where psychologic factors either predominate or are the sole cause of the patient's illness, the physician must determine whether he is willing and sufficiently competent to treat the patient, or whether he should refer him to a psychiatrist. . . . Harm can be done by a faulty psychosomatic approach, and very often patients will resent a purely psychosomatic approach and will not return. Most of the time it will be necessary to continue allergic therapy while trying to break through to the patient's emotional problem. . . . This should not even be attempted unless the physician has the time and the ability to handle such a problem. Above all, the alert allergist should be able to distinguish the true allergic patient from the so-called para-allergic. By so doing, no patient need be subjected to unnecessary psychotherapy or to prolonged and unnecessary allergic therapy.—Samuel S. Burden, M.D., The Role of the Psyche in Allergic Disease, *Annals of Internal Medicine*, December, 1955.

BILATERAL AND RECURRENT RENAL CALCULI

EVIDENCE INDICATING RENAL COLLAGEN ABNORMALITY AND RESULTS OF SALICYLATE THERAPY

Roger Baker, M.D.
and
John P. Connelly, M.D., Washington, D. C.

• A study of 357 patients with well-established diagnoses of renal calculus showed that in 9 instances of unilateral calculus there followed recurrence in the same kidney while in 12 instances recurrence was in the contralateral kidney. Bilateral recurrence was seen in eight cases after an initial unilateral calculus, and in four instances after an initial bilateral calculus. Urine cultures were sterile in 43% of patients with bilateral and recurrent calculi, so that infection could not be proved to be the cause of the lithiasis. Needle biopsies of both kidneys in a small series of patients revealed alterations of the connective tissue matrix about the renal tubules. This finding, together with the foregoing facts about bilaterality and recurrence, suggest that renal lithiasis may be a systemic disorder belonging to the group of collagen diseases.

It is the purpose of this paper to review the literature concerning incidence of recurrent and bilateral renal calculi and to report a study of two representative series of patients. These data are necessary for several reasons. From a clinical standpoint, certain aspects of the subject have not been reviewed since 1940. As a consequence, the influence of recent laboratory emphasis on establishing etiology and the effect of newer therapeutic procedures or drugs on renal calculus disease have not been evaluated. In addition, factual information should be available to the physician concerning the percentage of patients with stone in whom an etiological process can be determined, the incidence of bilateral occurrence, the incidence of recurrence and time factor relative to this recurrence, and any statistical evidence concerning infection in these patients. Probably of greater importance from the standpoint of investigation into the nature and mechanism of calculus disease is the question of whether recurrence of stone occurs as frequently in the contralateral as in the ipsilateral kidney. Stone formation is not simply a question of crystal precipitates falling out of a supersaturated urine; urinary crystals remain as crystals until they adhere to each other. Various evidence suggests that urinary crystals must be stuck together by some protein-sugar compound (mucoprotein) in order to form a stone. The presence of this mucoprotein has been shown by Rubin and Howard [1] in all types of calcific renal stones except calcium oxalate. Refinements of our present crude techniques may permit its identification in this type of stone as well. It is probably pertinent that in the normal calcification in bone the same process of deposition of calcium in cartilage mucoprotein takes place.

While the precise chemical structure of urinary mucoprotein in patients with calculus disease remains unknown, it has been isolated by Boyce and associates [2] and observed by others through electromicroscopy. It is known to be of such high molecular weight that it is unreasonable to consider that its presence in the urine is the result of filtration through the glomerulus or of secretion or excretion by the renal tubule. Apparently this mucoprotein is formed within the urinary tract in renal calculus disease. Reports published from this laboratory [3] have demonstrated alterations of the renal tubule connective tissue mucoprotein immediately preceding calcification in rats. This has been observed consistently with four different methods of producing experimental renal calculi. Subsequently calcification or stone formation occurs in this altered mucoprotein whether within the kidney (nephrocalcinosis) or the renal pelvis or urinary bladder (renal or bladder calculus). As a result of these and other observations, it is our impression that formation of urinary tract calculi may not be a disease of urine but rather a systemic condition specifically involving the normal connective tissue matrix of both kidneys. If this hypothesis is correct, then recurrence of renal calculi should be associated with stone formation as frequently in the contralateral as in the ipsilateral kidney except in cases where known local factors such as unilateral ureteral obstruction result in stone formation in one kidney. No publications have been found in the literature concerning site of recurrent renal stone formation. These statistics are now presented in this paper.

Methods

The first step toward fulfilling these objectives was a review of the literature regarding recurrent and bilateral renal calculi since 1915. Next, a survey was made of all patients with renal calculi at Georgetown University Hospital for the period of 1949-1954. Regardless of the fact that consecutive cases were studied, this series is per force selective, as all of these patients were from a private hospital; therefore, to provide a valid investigation a similar study was made of indigent patients from the District of Columbia General Hospital. This period covers the years when many of the present antibiotic drugs and chemotherapeutic agents were in active clinical use. It also covers the period when the chemistry laboratory has been most active in diagnosis of metabolic and endocrinous disorders as well as the period when so-called dietary management was used in an attempt to reduce recurrence of calculi. Only those patients satis-

From the Department of Surgery (Urology), Georgetown University School of Medicine.

Read before the Section on Urology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1955.

This study was supported in part by a grant from the United States Public Health Service and the American Urological Research Foundation.

The Fizrim (effervescent aspirin powder) used in this study was supplied by the Sterling-Winthrop Research Institute, Rensselaer, N. Y.

fying one or more of the following criteria were included in these series: (1) radiographic evidence of calculus, (2) history of urinary tract calculus with operative removal, or (3) cystoscopic evidence of nonopaque stone by passage of ureteral catheter to the calculus. Excluded from the series were patients with history of repeated bouts of renal colic with questionable passage of a stone and those in whom a roentgenogram was not taken after the passage or surgical excision of a stone in order to exclude the possibility of multiple calculi. These criteria excluded many patients from the series, but significant results were not otherwise possible. The cases of 256 patients fulfilling these specifications at Georgetown University Hospital and 101 from the District of Columbia General Hospital were reviewed.

Results

A survey of the literature presenting the incidence of renal stones appearing bilaterally is tabulated according to years in table 1. It is evident that the incidence of bilateral renal calculi has decreased slightly in the last 20 years. The literature further reveals that the recurrence rate (table 2) of renal calculi has decreased; however,

TABLE 1.—*Incidence of Bilateral Renal Calculi*

Year	Observer	Results, %
1917	Kummel	16.0
1918	Bevan	20.0
1918	Braasch	12.3
1924	Chute	18.0
1925	Thomas	12.0
1927	Kuster	11.0
1934	Winsbury-White	13.0
1938	Andres	16.4
1938	Morl	13.9
1939	Parmenter	8.0
1954	Baker and Connelly	8.0

it has remained, as of 1940, at 8%. There is one report, published in 1939,[4] of a much lower percentage (4.7). As this rate of calculus recurrence is so low and is at such variance with all other published work, it has not been included in table 2 and deserves separate discussion. That paper evaluated vitamin A deficiency and acid or alkaline-ash diets from the standpoint of recurrence of stones. Since antibiotic drugs and chemotherapeutic agents were not generally available at that time, it excludes their influence. If these clinical data are confirmed by others, then it will be necessary to reopen for further study the entire field of vitamin A deficiency and acid and alkaline-ash diets in relation to genesis and treatment of stone recurrence. Certain recent laboratory evidence warrants renewed investigation into the mode of action of vitamin A at this time.

Of the patients with calculus disease at both the District of Columbia General Hospital and Georgetown University Hospital, 8% had bilateral renal stones on admission. This is the same rate as that obtained in 1939. There was a 9% incidence of patients having recurrence of renal calculi after passage or removal of stone. This figure would seem to reflect a marked decrease in the incidence of recurrence of stones when compared to statistics obtained since 1915 (table 2). Upon closer inspection, however, the recurrence rate of 9% is only slightly lower than that given in the report by Braasch and Foulds 30 years ago (10.8%).

After compiling the statistics for this paper, we were surprised to learn that there was such close approximation of the results from two independent hospitals representing different social and racial groups, private and

TABLE 2.—*Incidence of Recurrence of Renal Calculi*

Year	Observer	Results, %
1915	Cabot and Crabtree	56.0 Postnephrotomy
1922	Barney	51.0 Postnephrotomy
1924	Chute	32.0
1924	Braasch and Foulds	10.79
1925	Thomas	33.0
1931	Herbst	15.0
1933	Higgins	16.4
1937	Brongersma	23.6 Postpyelotomy 35.4 Postnephrostomy
1937	Twinem	20.9 Postpyelotomy 28.0 Postnephrostomy
1940	Twinem	8.0
1954	Baker and Connelly	9.0

indigent patients. This correlation can be seen in table 3. Further breakdown of the data regarding time interval of recurrence and percentage of recurrence in the same and opposite kidneys among patients at both hospitals reveals approximately the same similarity (table 3). It was learned that if a patient developed a stone in one kidney and subsequently had a recurrence there was more than a 50% chance that the stone would develop in the opposite kidney. The data indicate that, once a calculus has passed or is removed, recurrence usually develops within three to five years. This conclusion was valid in over two-thirds of the patients studied (24 out of 33 patients). Recurrence is infrequent after eight years have passed since the original attack.

Possible etiological factors concerned in these series were varied, but the fact that infection formed the main bulk of genitourinary pathology associated with renal

TABLE 3.—*Recurrent Renal Calculi in Patients Seen at Georgetown University Hospital and District of Columbia General Hospital*

	Patients, No.		Mean Time, Months		Range, Months	
	G*	D*	G*	D*	G*	D*
Unilateral stone; recurrence in same kidney	8	1†	37.4	38.5	9-79 (252)‡	17-60‖
Unilateral stone; recurrence in opposite kidney	9	3	30.4	44.3	4-84 (256)‡	24-60
Unilateral stone; bilateral recurrence	3	5	88.0	80.8	24-180	17-204
Bilateral stones; bilateral recurrence	3	1	30.3	120.0	21-35	.....

* G = Georgetown University Hospital. D = District of Columbia General Hospital.
† This patient also developed a stone in the opposite kidney after recurrence in the same kidney.
‡ Not included in further statistics due to marked variation from other figures.
‖ Recurred in same patient at these time intervals.

stones warrants consideration. Of all patients studied who had recurrent or bilateral renal calculus disease, 50% had associated acute or chronic pyelonephritis. What is probably of more importance is the fact that 43% of the patients in this series had sterile urine cultures. Unfortunately, 2% of the charts failed to contain a report of urine culture. When viewed from a most

liberal standpoint, determined etiological factors in the series now reported of bilateral or recurrent calculi include: obstructive uropathies (5 of 55 cases, or 9%); systemic diseases such as gout, rheumatoid arthritis, and poliomyelitis with prolonged bed rest (6%); and hyperparathyroidism with nephrocalcinosis or renal calculi (5.4%). Definitive etiology could be determined, therefore, in a maximum of only 20.4% of this group, or, to put it more meaningfully, there was no demonstrable etiology in 79.6% of patients with bilateral or recurrent renal calculus disease. This affords an idea of the extent of the research problem still remaining.

Comment

These data have value both clinically and in research. From a clinical point of view, it is important to be aware that in patients with signs and symptoms of a unilateral renal calculus there is an 8% chance that a calculus may be present also in the opposite kidney. If the patient has a renal stone removed or passes it spontaneously, the likelihood of its recurrence is about 9%. Apparently this is a fairly constant incidence rate for the year 1955; Prince and co-workers [5] report 8.8% in the same year. Contrary to popular opinion, the facts indicate that stone recurrence is apparently just as frequent in the contralateral kidney as in the kidney that developed the original stone. In addition, if the patient is to have a recurrence, it will usually appear within three to five years, but it may develop as late as eight years after the first episode. Recurrence is infrequent after this.

Infection.—The absence of infection in 43% of patients with recurrent or bilateral renal calculus disease is further support for the premise that infection is probably either a contributing factor to stone formation or a result of local irritation rather than a primary cause of the condition. These statistics tend to confirm the study published by Rovsing [6] in which he reported that the urine was sterile in 56% of 716 patients with renal calculi. It is logical to find that in a series of bilateral and recurrent calculi the incidence of sterile urine would be lower. Bell [7] studied 115 cases of renal tuberculosis but found that only three patients with this specific infection developed calculi.

There is no conclusive published evidence that infection, per se, is the etiological factor in human calculus disease. It is granted that recurrent pyelonephritis due to gram-negative organisms thriving in an alkaline urine has considerably more than a chance association with calculi. The fact is that only a very small percentage of patients with acute or chronic pyelonephritis actually develop calculi, and approximately one-half of all patients with renal calculi have no infection. This apparent inconsistency with popular medical opinion remains unexplained unless the conclusion be accepted that pyelonephritis is not the cause of renal calculus disease. Without doubt, renal infection of a particular type is probably a contributing factor or the trigger mechanism necessary for activation of some stone-forming process already present. For example, current studies show that it is extremely rare to find calcification induced by injection of Proteus vulgaris into the bladder of the rabbit. This organism, however, readily leads to production of stone in the bladder when there has been some chemical or physical trauma to the mucosa or a foreign body has been inserted within the bladder to irritate the vesical mucosa.

Etiology.—It has been stressed repeatedly in the medical literature that gross abnormalities in calcium metabolism resulting in hypercalcemia and hypercalciuria, as in hyperparathyroidism, can be a major factor in the production of calculi. Reference to published facts indicates that about 50% [8] of patients with hyperparathyroidism actually develop renal calculi. It is also commonly accepted that the etiological factor in many patients with calculi is obstructive uropathy, dehydration, or systemic diseases such as gout, cystinuria, or obligatory prolonged bed rest. Critical appraisal of these so-called known causes of stone formation reveals that the vast majority of patients with any one of them never develop renal calculi. For example, while many patients with gout have renal impairment, only 11 to 23% have stones or gravel. Of patients having obstructive uropathy, only 7 to 10% have calculi.[9] Of 800 recumbent patients studied for an average time of approximately one year, only 2% formed urinary calculi.[10] Conclusions from these facts are twofold: first, in the bulk of cases the etiology of stone formation is obscure, and, second, in the small group of patients in whom the "etiological" factor appears known, it has only been suspected but not proved as a true etiological factor. More often than not, if approached from another aspect it could just as reasonably be stated that the renal calculus in such a situation is an inconsistent renal complication of the condition. Factual data proving causation are sketchy. Some or all of these factors may be truly causative. This applies particularly to hyperparathyroidism, where removal of an existing lesion such as an adenoma usually prevents stone recurrence. At the present writing most of these factors must be considered as only contributory processes; for example, they were found in only one-fifth of the patients having bilateral and recurrent calculi in the two series now reported.

Evidence Indicating Collagen Abnormality in Renal Calculosis.—It cannot be taken for granted that hyperexcretion of certain urinary crystals or crystalloids or calcium will cause a stone per se. It is possible but not probable that a patient may have a stone solely as the result of hyperexcretion of these elements, but most valid data fail to support this concept. Excess saturation of urine or any other solution with a crystal causes crystals (not a stone) to drop out of the solution. It has been reasoned by any number of authors that these crystals serve as a "nidus" or "nucleus" for subsequent deposition of crystals or salts, thus forming a stone. The critical factor in this popular concept of stone genesis is the presence of some cohesive substance in the urine that causes these crystals or salts to adhere to the nidus and also to each other. All significant published evidence indicates this cohesive substance to be a mucoprotein. Furthermore, it is an irrefutable fact that overloading of the urine with crystals is not essential to stone formation. Most patients with hypercalcemia, hypercalciuria,

or hypercrystalluria never develop a calculus, and most patients with a urinary tract calculus do not have hypercalcemia, hypercalciuria, or hypercrystalluria. It is certainly possible that patients might develop a specific type of renal injury from an abnormally high renal excretion of calcium or crystals. This renal injury may cause conversion and release or excretion of a specific renal mucoprotein into the urine that binds the calcium salts or crystals to each other or on a nidus. This area requires further study.

It is common belief that stones will recur in the kidney that was first attacked. The data obtained by this investigation failed to support this concept. Of 28 patients who had recurrent unilateral renal calculi, there were more recurrences in the contralateral kidney (12 patients) than in the ipsilateral kidney (8 patients) or in both kidneys (8 patients). These results support the suggestion that renal calculosis is apparently a systemic condition specifically affecting both kidneys and the causative factor is not necessarily a local or urinary abnormality. These observations have prompted an additional study that is in progress. Needle biopsy specimens of both kidneys have been obtained from a small series of patients with unilateral renal calculi, and they reveal bilateral alterations of the renal tubule connective tissue matrix or mucoprotein.[11] These data tend to correlate and substantiate the hypothesis developed in this laboratory that most kidney stones represent renal collagen disease—that is, a disease of the tubule connective tissue matrix or mucoprotein.

As mentioned previously, stones are apparently a conglomeration of crystals held together by a matrix of mucoprotein. This mucoprotein has been observed for all types of calcific renal stones except calcium oxalate with the extremely crude Hotchkiss periodic-fuchsin technique.[1] Refinement of existing techniques may reveal its presence in calcium oxalate stones as well. Boyce and others [2] and Porter [11a] have demonstrated the presence of mucoprotein in the urine of patients with calculi. The great size of the molecule precludes passage through the glomerulus, thus indicating that it must be formed at a lower level in the nephron. Studies from our laboratory have shown bilateral precalcific alterations in renal tubule mucoproteins with four different methods of producing experimental calculus disease.[3] Subsequent calculous matter was deposited in this altered mucoprotein, either in the renal tubule (nephrocalcinosis) or after it has been exuded within the tubule and deposited in the urine of the calyx or renal pelvis (renal calculus). Similar renal tubule mucoprotein abnormalities have been reported in patients with calculus disease.[3b] The specific nature of this connective tissue abnormality is unknown. It is known, however, that the glomerulus is not involved in the process. The results now presented show that most patients with a kidney stone appear to have bilateral renal disease, as recurrence is as frequent in the opposite kidney as in the kidney originally attacked. Furthermore, in the patients studied to date, unilateral renal or ureteral calculi are associated with connective tissue matrix disease of the tubules in both kidneys.

The calcium of normal bone is deposited within changed or depolymerized mucopolysaccharide, which converts it to a calcium-bindable mucoprotein. The same process takes place in the calcification of costal cartilage. In arteriosclerosis earliest calcification occurs in the connective tissue matrix of the subintimal layer. In early osteoarthritis, depolymerization of the mucopolysaccharide converts it to mucoprotein. Earliest calcification appears in this mucoprotein. Evidence is accumulating that shows that pathological calcification, including the renal variety, is a disease of the connective tissue matrix. As such, it is essentially a collagen disease in the true sense of the word. When appraising the problem of renal calculus disease from this standpoint, the following factors are necessary for calcification: 1. Calcium and phosphorus must be available in the serum or urine, but clinical and experimental evidence has shown that it is not necessary to stone formation that they be present in quantities either greater or less than normal. 2. An etiological factor is necessary to specifically convert the renal tubule connective tissue matrix or mucopolysaccharide to a calcium-bindable mucoprotein. 3. Specific contributory factors are needed. These include such conditions as dehydration, specific infections, increased intake of dairy products, hypercalcemia, hypercalciuria, prolonged bed rest, and obstructive uropathy. They serve to trigger the basic mechanism in a patient who is already disposed to stone formation. The vast majority of persons with one or more of these contributory factors never develop calculi. These factors result in stone formation only when they are combined with some other specific process as yet not defined. 4. Time is needed for the development of calculi.

Treatment.—The principal present medical management used in an attempt to prevent stone recurrence is an attack upon two of these areas by (1) decreasing calcium and phosphorus concentration or availability and/or altering the solubility of these substances, or (2) eliminating a determined contributory factor. The first is accomplished by such methods as decreasing excessive intake of dairy products, use of aluminum gels, excision of parathyroid adenomas, decreasing concentration by hydration, altering pH to change solubility, passive or active motion of bedridden patients to reduce demineralization of bone, and use of chelating agents to tie up calcium. Contributory factors such as infection are treated by administration of appropriate antibiotic or chemotherapeutic drugs. Obstructive uropathy is relieved surgically. Treatment of the etiological factor is difficult, as little is definitely known of this facet of the problem. Treatment of an etiological factors can be effective in hyperparathyroidism and is under study by various groups in the diseases of gout and cystinuria.

On the basis of the evidence presented above, this paper suggests another area for treatment in renal calculus disease: the altered tubule connective tissue mucoprotein. Our experience with "anti-inflammatory" drugs in treatment of animals with a known incidence of calculi and in a study of patients with recurrent stones has been identical to that obtained with these same drugs in treatment of other collagen diseases such as rheumatic fever and arthritis.[12] These experimental stud-

ies showed that treatment with acetylsalicylic acid (aspirin), small doses of cortisone acetate, other corticosteroid hormones, phenylbutazone (Butazolidin), and corticotropin (ACTH) reduces recurrence rate of stones nearly 50%. Certain patients develop annoying or distressing symptoms while taking 1-2 gm. of aspirin each day. One such patient had activation of a quiescent duodenal ulcer while on long-term aspirin therapy. Because of these complications, alkalizing salicylates such as Fizrim (effervescent aspirin powder) are now used.

Snapper, Bendien, and Polak [13] showed in 1936 that sodium salicylate inhibits precipitation of urinary colloids. This concept of action is more tenable than is the assumption that inhibition of stone recurrence is simply an effect of decreasing urinary pH by daily administration of large amounts of acetylsalicylic acid. Other investigators [14] explain this effect from another related stand, contending that salicylates increase urinary glucuronide concentration, which in turn increases solubility of calcium phosphate. While it is possible that this is an explanation for the inhibition of stone formation observed in our study, it is not completely compatible with other observations. For example, it is known that administration of salicylates to patients with gout alters the rate and amount of uric acid crystals excreted in the urine. Our studies, as well as other studies of this type, have failed thus far to find a patient with gout develop or have recurrence of demonstrable uric acid stones while receiving large daily doses of salicylates. The urinary solubility of calcium phosphate is, therefore, not important or pertinent in this group of patients. In controlled experiments renal tubule mucoprotein alterations routinely preceded four different types of calcification; calcific matter was subsequently deposited in them. Salicylates or small doses of cortisone acetate caused a significant reduction in these alterations of renal tubule connective tissue matrix, and subsequently less nephrocalcinosis or production of renal calculi was observed.

As in other collagen diseases, little or no additional effect was accomplished by combining drug therapies mentioned above. Cessation of therapy with the drug or drugs was associated with the same rate and severity of recurrence of renal calculi that existed prior to institution of therapy. This was expected, since the etiological factor had not been eliminated. As the statistics presented in this paper indicate, it is fortunate that 91% of patients with a calculus never have a recurrence. For those patients who do, this therapeutic area warrants trial and further investigation.

Summary and Conclusions

On the basis of a study of 356 patients with evidence or a history of renal calculi, the following conclusions have been made. Eight per cent of patients with stone in one kidney also have a stone in the other kidney when first examined. Nine per cent of patients who have a stone develop a recurrence in the same or opposite kidney. There was no evidence of infection in 43% of patients with bilateral and recurrent calculi. There was no established etiology in 79.6% of patients with bilateral and recurrent calculi. Support for the theory that renal lithiasis is probably a bilateral renal disease is indicated by the fact that there are somewhat more recurrences of renal calculi in the contralateral than in the ipsilateral kidney. Bilateral renal biopsy revealed abnormal tubule connective tissue matrix of both kidneys in patients with unilateral calculus disease. There is evidence indicating that renal calculosis should be considered a connective tissue collagen disease. Treatment with "anti-inflammatory" drugs reduces the recurrence rate of calculi nearly 50%.

3800 Reservoir Rd. (Dr. Baker).

1. Rubin, P. S., and Howard, J. E.: Histochemical Studies on the Role of Acid Mucopolysaccharides in Calcifiability and Calcification, Transactions of the 2nd Conference on Metabolic Interrelations, New York, Josiah Macy, Jr. Foundation, 1950, p. 155.

2. Boyce, W. H.; Garvey, F., and Norfleet, C.: Ion-Binding Properties of Electrophoretically Homogeneous Mucoproteins of Urine in Normal Subjects and in Patients with Renal Calculus Disease, J. Urol. **72**: 1019-1031 (Dec.) 1954.

3. Baker, R.; Reaven, G., and Sawyer, J.: (*a*) Ground Substance and Calcification: The Influence of Dye Binding on Experimental Nephrocalcinosis, J. Urol. **71**: 511-521 (May) 1954; (*b*) Effect of Toluidine Blue on Metastatic Calcification, Proc. Soc. Exper. Biol. & Med. **83**: 281-284 (June) 1953; (*c*) Baker, R., and Sison, F.: Demonstration of Altered Tissue Mucopolysaccharides in Renal Calculus Disease by Selective Staining Techniques, J. Urol. **72**: 1032-1045 (Dec.) 1954.

4. Higgins, C. C.: Factors in Recurrence of Renal Calculi, J. A. M. A. **113**: 1460-1465 (Oct. 14) 1939; Recurrent Renal Lithiasis, Cleveland Clin. Quart. **6**: 18-28 (Jan.) 1939.

5. Prince, C. L.; Scardino, P. L., and Wolan, C. T.: The Effect of Temperature, Humidity and Dehydration on the Formation of Renal Calculi, J. Urol., to be published.

6. Rovsing, T.: Kidney Calculi, Ztschr. f. Urolog. Chir. **12**: 358-384 (March) 1923.

7. Bell, E. T.: Renal Diseases, Philadelphia, Lea & Febiger, 1947.

8. Alexander, H. B.; Pemberton, J. deJ.; Kepler, E. J., and Broders, A. C.: Functional Parathyroid Tumors and Hyperparathyroidism, Am. J. Surg. **65**: 157-188 (Aug.) 1944.

9. Baker, R.; Kennelly, J., and Kelly, T.: Obstructive Uropathy and Calculus Disease, unpublished data.

10. Kimbrough, J. C.; Denslow, J. C., and Worgan, D. K.: Urinary Tract Calculi in Recumbent Patients, J. A. M. A. **142**: 787-789 (March 18) 1950.

11. Baker, R., and others: Bilateral Renal Needle Biopsy of Patients with Unilateral Renal Calculi: A Preliminary Report, unpublished data.

11a. Porter, K. R., and Tamm, I.: Direct Visualization of a Mucoprotein Component of Urine, J. Biol. Chem. **212**: 135-140, 1955.

12. Baker, R., and Flynn, W.: Salicylate Inhibition of Experimental Renal Calculus Disease, Proc. Soc. Exper. Biol. & Med., to be published.

13. Snapper, I.; Bendien, W. M., and Polak, A.: Observations on the Formation and the Prevention of Calculi, Brit. J. Urol. **8**: 337-345 (Dec.) 1936.

14. Prien, E. L., and Walker, B. S.: Use of Salicylamide and Acetylsalicylic Acid in Recurrent Urolithiasis, J. A. M. A., to be published.

Vertigo.—The real essential of vertigo is the sense of movement, primarily of turning as the term implies. This movement is generally of surrounding objects, but one does meet the occasional patient with a true vertigo who interprets his sense of movement as being of himself. These cases, however, need to be accepted with reserve and the sensations carefully analysed: thus, with a patient who feels his head actually spinning round it may be a vertigo, but if he says he feels a spinning inside his head, it is probably not. Associated with the sense of movement is a disorder of equilibrium: from a mild, barely noticeable lurch to the patient being thrown violently to the floor. Accompanying the vertigo is nausea or vomiting and the severity of this is directly proportional to the severity and duration of the vertigo: only in the shortest and mildest episodes is it really absent and in any sharp attack the vomiting is a prominent feature. Intelligent patients will often grade their attacks according to the amount of sickness. This close correlation is often a useful diagnostic point as, although one may well vomit with a variety of conditions, this gradation only occurs with a true vertigo. Another typical point about many cases of vertigo is the association of the vertigo with head movements. In a mild attack or when a vertigo is settling down, it will often be brought on again by quick side-to-side movements of the head. This is probably the reason why these patients find streets and traffic so unpleasant, the almost instinctive quick look both ways before crossing a street being quite enough to disturb the precarious equilibrium of their labyrinths.—N. S. Alcock, M.D., F.R.C.P., The Clinical Significance of Vertigo, *The Practitioner*, February, 1956.

COMPLETE NUTRIMENT FOR THE THERAPY OF PEPTIC ULCER

Asher Winkelstein, M.D.
and
Eric Schweiger, M.D., New York

• A fluid nutriment (Sustagen) of known carbohydrate, fat, protein, mineral, vitamin, and known caloric content was tested to determine whether its effects on gastric acidity might render it useful in patients with various gastric secretory disturbances.

Sustagen provoked less secretion of acid than did a test meal of crackers and water in 10 patients. It suppressed the secretion of free acid in response to histamine in four patients. A group of four patients took it alternately with milk on successive days; gastric analyses showed that the Sustagen caused more complete and prolonged reduction of acidity than did the milk. A group of six patients who had been suffering from the distressing symptoms of prolonged nocturnal hyperchlorhydria received Sustagen by continuous intragastric drip, which completely abolished the free acidity during the night.

The underlying or ultimate cause of peptic ulcer is as yet unknown. Today there are many observers who think the cause resides in an emotional disturbance; however, it is generally agreed that the immediate cause of ulceration is peptic, i. e., the effect of free hydrochloric acid and pepsin on a susceptible mucosa. As a result of this concept, most ulcer therapies attack the "acid" or "peptic" factor. For this purpose, a therapy that provides a bland, high-caloric fluid, and that also possesses good neutralizing properties, would seem to constitute an ideal ulcer therapy.

Recently a high-caloric nutrient powder, Sustagen, has appeared, that may be preeminently satisfactory for that purpose. Sustagen has been utilized for the nutritional therapy of debilitated patients, particularly in the form of liquid tube feedings. Sustagen is produced in powder form and is easily mixable in water to form a liquid emulsion. One hundred grams of Sustagen supply 390 calories, 24% of which are from protein, 8% from fat, and 68% from carbohydrate. In addition, it contains the essential vitamins and minerals. An analysis of the properties of this agent suggested to one of us (A. W.) the idea that this preparation might prove of considerable value in the care and dietary treatment of patients with peptic ulcer.

The characteristics of this material that suggested its use in ulcer therapy are as follows: (1) fluid nature, (2) palatability, (3) high-caloric value, (4) complete mineral and vitamin supplement, and (5) probable acid-neutralizing effect. Since modern peptic ulcer therapy depends largely on the neutralization of the gastric acid secretions, it was decided to investigate the neutralizing ability of Sustagen in patients with a wide variety of gastric secretory disturbances. Among these were patients with duodenal ulcer (with nocturnal hypersecretion) and hiatus hernias. In addition, since the conventional dietary therapies of ulcer rely mainly on the administration of milk, based on similar considerations, it was therefore decided to include a study of the antacid effect of Sustagen as compared with that of milk.

Methods

Thirty patients from the wards and outpatient clinics of the Mount Sinai Hospital were studied. These patients all had upper gastrointestinal complaints. Gastric analysis was done as part of the routine study. Twelve patients had duodenal ulcer proved radiographically. The nocturnal secretory activity in five of these cases was studied, and hypersecretion and hyperchlorhydria was found. Four patients had a hiatus hernia; one had carcinoma of the fundus of the stomach; and two had chronic gallbladder disease. These seven patients also had gastric acid hypersecretion. In the absence of a definitive diagnosis, the remaining 11 patients were classified as having conditions that were functional in origin.

Gastric contents were obtained by means of nasogastric aspiration with the use of a small caliber Levin tube. The amount of hydrochloric acid was determined by titration, with Töpfer's reagent as the indicator of free acidity. The patients were divided into four groups.

Group 1.—Of 16 patients with varying fasting gastric acidity, 10 (table 1) received a routine test meal consisting of three arrowroot crackers and 240 cc. of water,

TABLE 1.—*Free Gastric Acidity (Clinical Units) Response to Test Meal and Sustagen*

			Standard Test Meal				240 Cc. of Sustagen Mixture Taken Orally					
Case	Diagnosis	Fasting 0 *	1	2	3	4	5	6	7	8	9	10
1	Chronic gallbladder disease	30	8	40	38	28	0	0	0	0	0	0
2	Duodenal ulcer	16	16	34	54	54	0	0	0	0	0	0
3	Functional	0	0	34	74	72	0	0	0	0	0	0
4	Functional	0	0	6	30	50	0	0	0	0	0	0
5	Duodenal ulcer	34	22	18	30	28	0	0	0	0	0	0
6	Duodenal ulcer	58	24	36	56	36	0	0	0	0	..	..
7	Functional	46	0	20	14	20	0	0	0	0	..	..
8	Functional	6	2	20	24	32	0	0	0	0	..	..
9	Functional	12	2	18	16	18	0	0	0	0	..	..
10	Duodenal ulcer	10	10	10	18	30	0	0	2	42	..	..
Av. gastric acidity		21.2	8.4	23.6	35.4	36.8	0	0	0.2	4.2	0	0

* 0 to 10 indicate testing periods, each equaling 15 min.

after which samples of the gastric contents were aspirated every 15 minutes for a period of one hour. At the end of one hour, 240 cc. of Sustagen mixture (135 gm. of Sustagen in 240 cc. of water) was swallowed by the patient. Gastric aspirations at 15-minute intervals were then continued for one to two more hours. After the aspiration of the fasting stomach contents for one or two 15-minute periods, the remaining six patients (table

From the Gastrointestinal Unit of the Medical Department of the Mount Sinai Hospital.

This study was supported by a grant from Mead Johnson & Company, Evansville, Ind.

2) also swallowed 240 cc. of Sustagen mixture. After this, all procedures were carried out as in table 1.

Group 2.—Four patients were given 0.5 mg. of histamine hydrochloride (1:1,000) subcutaneously, after which samples of the stomach contents were aspirated at 15-minute intervals for one hour (table 3). Then

TABLE 2.—*Free Gastric Acidity (Clinical Units) Response to Sustagen*

		Fasting		240 Cc. of Sustagen Mixture Taken Orally							
Case	Diagnosis	0 *	0′	1 †	2	3	4	5	6	7	8
11	Functional	40	54	0	0	0	4	4	4	0	0
12	Carcinoma, stomach	..	30	0	0	0	0	6	6	26	24
13	Hiatus hernia	..	40	0	0	0	0	0	0	0	..
14	Functional	..	54	20	0	0	0	0	0	0	0
15	Hiatus hernia	..	10	0	0	0	0	0	0	0	..
16	Functional	10	20	0	0	0	..	0	0	0	..
Av. gastric acidity		25	34.7	3.3	0	0	0.8	1.7	1.7	4.3	8

* 0 and 0′ are two fasting aspirations at 15-min. intervals.
† 0 to 8 indicate testing periods, each equaling 15 min.

240 cc. of Sustagen mixture was swallowed by the patient. Gastric aspiration was continued every 15 minutes for an additional hour.

Group 3.—Four patients in a fasting state received 240 cc. of whole milk and 240 cc. of Sustagen mixture on alternate days. After the ingestion of either fluid, gastric aspiration was carried out at 15-minute intervals for a one and one-half to two-hour period (table 4).

Group 4.—Six patients with prolonged nocturnal hypersecretion and hyperchlorhydria were studied after ingestion of the standard arrowroot cracker and water test meal in the evening. Specimens of the stomach contents were obtained at hourly intervals during the night for periods ranging from three to seven hours by means of an indwelling nasogastric tube. The next night the same group of patients received a continuous intragastric Sustagen drip (450 gm. of Sustagen in 1,000 cc. of water) at the rate of 80 to 100 drops per minute. Samples of the gastric contents were again aspirated every hour for three to seven hours.

Results

Group 1.—Before the oral administration of the Sustagen mixture, nine patients in group 1 had free acid ranging from 40 to 74 clinical units, five patients had free acid

TABLE 3.—*Free Gastric Acidity (Clinical Units) Response to Histamine and Sustagen*

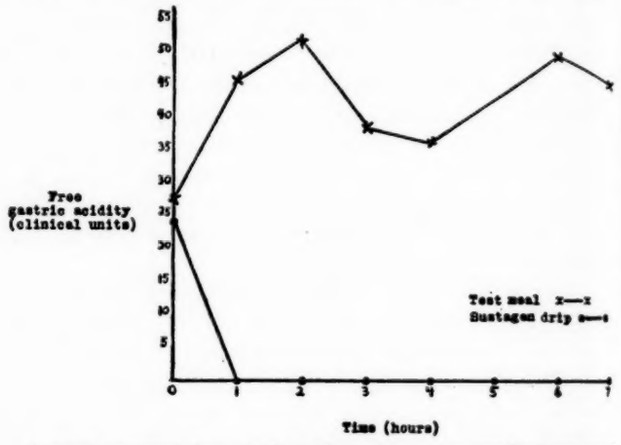
		Fasting	Histamine, 0.5 Mg. Given Subcutaneously				240 Cc. of Sustagen Mixture Taken Orally			
Case	Diagnosis	0 *	1	2	3	4	5	6	7	8
17	Functional	40	34	60	74	36	0	0	0	0
18	Hiatus hernia	16	34	66	70	68	0	0	0	0
19	Hiatus hernia	0	10	50	36	20	0	0	10	0
20	Chronic gallbladder disease	0	0	50	54	42	0	0	0	0
Av. gastric acidity		14	19.5	56.5	58.5	41.5	0	0	2.5	0

* 0 to 8 indicate testing periods, each equaling 15 min.

from 20 to 39 units, and two patients had free acid from 10 to 19 units (tables 1 and 2). In all of these 16 patients, after the oral administration of Sustagen, free hydrochloric acid was neutralized for periods ranging from one to two hours, with the exception of one patient, in whom free gastric acid had reappeared at the end of one hour. In 9 of the 11 patients who were studied for one and one-half hours, the free gastric acidity was completely controlled during the one and one-half hour period (tables 1 and 2).

Group 2.—After histamine injections, the four patients in group 2 showed free acid values ranging from 50 to 74 clinical units. After the oral administration of Sustagen mixture, no free acid was demonstrable in four subsequent gastric specimens obtained over a one-hour period from three patients. In the third aspiration, only a slight degree of free acid (10 units) appeared in one patient (table 3).

Group 3.—Free hydrochloric acid measured in the fasting stomach ranged from 34 to 62 clinical units in the four patients in group 3. After 240 cc. of whole milk was swallowed, a transient decrease in free acidity occurred; however, this drop never exceeded 55% of any fasting value and was not sustained beyond a one-half hour period. In all four patients, the free acid measured one hour after the milk was taken was actually higher than the fasting value. This secondary rise varied from 10 to 75% above the fasting values. The next day, the free acid as measured in the fasting state ranged



Average nocturnal free gastric acidity response to standard test meal and continuous intragastric Sustagen drip on alternate nights. Test substance given immediately after aspiration of fasting (0) specimen.

from 30 to 64 clinical units in the same four patients. Then 240 cc. of Sustagen mixture was taken by mouth by each patient, and either no free acid or merely traces were demonstrated for the subsequent one and one-half hour period. Two patients showed no free acidity for one and one-half hours, and only traces of free acid were recorded for the other two after Sustagen was swallowed (table 4).

Group 4.—After the evening test meal, all six patients in group 4 showed elevated free acid values ranging from 36 to 78 clinical units over a three to seven-hour nocturnal period. The next night, with continuous intragastric Sustagen drip, free hydrochloric acid in all six patients was effectively neutralized for the entire three to seven-hour period of hourly study (see figure).

Comment

Group 1.—It is apparent from the studies of the material in group 1 that the oral administration of 240 cc. of Sustagen mixture virtually abolished the free hydrochloric acid for periods ranging from one to two hours. Of 11 patients who were studied for a one and one-half

hour period, 9 patients showed complete control of free gastric acidity over that period.

Group 2.—After the subcutaneous injection of histamine, the same neutralizing effect of Sustagen on gastric acidity for a one-hour period was noted in four patients exhibiting high free acidity.

Group 3.—In view of the fact that milk is the standard and basic dietary therapy in peptic ulcer, it was thought that a comparative study of the effects of milk and Sustagen on gastric acidity should prove of special interest to those concerned with the dietary management of peptic ulcer. In four patients, to whom 240 cc. of whole milk was given, only a transient decrease in free acid occurred. It never went below 55% of the fasting values. It is of interest that, after the first hour of sample-taking, the free acid was actually higher than it had been with the patients in the fasting state; however, with equal amounts of Sustagen, free hydrochloric acid was virtually neutralized for one to one and one-half hours.

Group 4.—Numerous investigators—Winkelstein,[1] Henning and Norpoth,[2] Val Dez,[3] Dragstedt and others,[4] Levin and others [5]—have demonstrated conclusively that the nocturnal secretion of hydrochloric acid in peptic ulcer is increased in both concentration and volume. Ulcer therapists generally agree that, because of the distressing night symptoms characterizing the course of active peptic ulcer, the control of nocturnal hypersecretion should be a great advantage.[6] This neutralization should also theoretically protect the open ulcer from acid irritation and peptic digestion during the night. It was, therefore, considered particularly important to study the effect of Sustagen drip on night acid secretion (which easily lends itself to drip therapy because of its milk-like physical properties). This form of drip therapy was carried out in six patients who, in control studies, revealed prolonged nocturnal hypersecretion and hyperchlorhydria. It was found that the continuous Sustagen drip abolished the free acid completely. Although Winkelstein and others [7] have found that the night intragastric drip of milk-soda mixture or diluted aluminum hydroxide gels controls the night secretion of acid adequately in ulcer patients, Sustagen seems preferable because of its equally good neutralizing properties plus its food-vitamin-mineral values.

As a result of these considerations, it is proposed to treat ulcer patients with Sustagen mixture, both orally and by the intragastric drip method. It seems probable that this form of alimentation is superior to other conventional methods of dietetic treatment of peptic ulcer. Sustagen is a complete aliment in a bland liquid form; it is easily mixed, palatable, and has excellent and prolonged buffering powers. It is apparently superior to whole milk in its neutralizing properties, in its prolonged effect, and in the absence of a secondary rise in the free hydrochloric acid. Accordingly, several patients whose condition was refractory to the conventional Sippy type of therapy have been treated with Sustagen given orally or by drip, or by both methods combined, and the results seem promising in this small group. There were no undesirable side-effects. A few patients complained of the sweet taste of the aliment. In view of the good effects, we advocate an intensive trial of Sustagen in the therapy of uncomplicated peptic ulcer.

TABLE 4.—*Free Gastric Acidity (Clinical Units) Response to Oral Ingestion of Milk and Sustagen Mixture* on Alternate Days*

Case	Diagnosis	Test Substance	0†	1	2	3	4	5	6	7	8
21	Functional	Milk	40	20	18	28	30	30	48	..	..
		Sustagen	50	0	0	0	0	0	0	0	40
22	Duodenal ulcer	Milk	36	24	24	32	36	..	42	..	..
		Sustagen	50	2	12	4	0	0	10	..	..
23	Duodenal ulcer	Milk	34	30	22	26	40	56	60	..	..
		Sustagen	30	0	0	0	0	6	14	20	50
24	Duodenal ulcer	Milk	62	36	32	46	60	72	70	..	..
		Sustagen	64	0	0	0	0	0	0	24	..
Av. gastric acidity		Milk	43	27.5	24	33	41.5	53	55	..	..
		Sustagen	48.5	0.5	3	1	0	1.5	6	14.7	45

* 240 cc. of each. † 0 to 8 indicate testing periods, each equaling 15 min.

Summary and Conclusions

The neutralizing properties of Sustagen, a high-caloric nutrient powder, were studied in a group of 30 patients, most of whom had gastric acid hypersecretion. In addition, the antacid ability of Sustagen was compared to that of whole milk. It was found that whole milk administered orally failed to control the gastric acidity to any comparable degree. The oral administration of Sustagen mixture is followed by achlorhydria for one to two hours (usually one and one-half hours), and the intragastric night drip of Sustagen produces a continuous absence of free hydrochloric acid. This excellent neutralizing property suggested use of Sustagen in the medical therapy of peptic ulcer. As a result of these studies, a clinical trial of Sustagen in the treatment of uncomplicated duodenal and gastric ulcer seems justified.

1185 Park Ave. (28) (Dr. Winkelstein).

1. Winkelstein, A.: Studies in Night Gastric Secretion with a Preliminary Note on a New Method of Therapy for Peptic Ulcer, Am. J. Surg. **15**: 523, 1932.

2. Henning, N., and Norpoth, L.: Untersuchungen über die sekretorische Funktion des Magens während des nächtlichen Schlafes, Arch. f. Verdauungskr. **53**: 64, 1933.

3. Val Dez, F. C.: Night Secretion of Free Hydrochloric Acid in the Stomach, Illinois M. J. **81**: 149, 1942.

4. Dragstedt, L. R.; Palmer, W. L.; Schafer, P. W., and Hodges, P. C.: Supra-Diaphragmatic Section of Vagus Nerves in the Treatment of Duodenal and Gastric Ulcers, Gastroenterology **3**: 450, 1944.

5. Levin, E.; Kirsner, J. B.; Palmer, W. L., and Butler, C.: Comparison of Nocturnal Gastric Secretion in Patients with Duodenal Ulcer and in Normal Individuals, Gastroenterology **10**: 952, 1948.

6. Winkelstein, A.: Modern Treatment of Peptic Ulcer, New York, Oxford University Press, 1948.

7. Cornell, A.; Hollander, F., and Winkelstein, A.: The Efficacy of the Drip Method in the Reduction of Gastric Acidity, Am. J. Digest. Dis. **9**: 332, 1942.

PROGRESS IN PREVENTION OF CHRONIC ILLNESS, 1949-1956

Leonard A. Scheele, M.D., Washington, D. C.

• The program of medicine is not preventive, or curative, or restorative alone, but all three together. Chronic disease develops as the result of the total life experience, from the moment of conception onward. More emphasis must be placed on the personal health of the younger age groups. Much chronic disability can be avoided by the prevention of accidents. The faulty methods of treatment that have contributed to chronicity and disability among the mentally ill can be corrected. Full application of what is already known about prevention and treatment would so reduce the burden of chronic disease as to mark an epoch in the economic, social, and medical history of the nation.

Seven years ago, I had the privilege of addressing the first meeting of the Commission on Chronic Illness. Today, I am sensible of the honor of speaking at the final meeting, but not without a certain feeling of regret. For I believe that no one concerned with the problems of chronic illness can contemplate the commission's absence from the national scene without wondering how the gap can be filled. Granted, it was not the aim of the commission to make a permanent place in the sun for itself. Its mission has been the very reverse of empire building. But the commission has made a place for itself—in hundreds of communities, institutions, and organizations across the country and in thousands of individuals, professional and public leaders alike. It will be remembered for a long time to come.

Seeking a common meeting place for the exchange of problems and ideas, many groups and individuals have participated in national conferences sponsored by the commission on the major aspects of chronic illness. Seeking information on subjects often inadequately explored in the past, they have profited by a series of important studies conducted or stimulated by the commission. Seeking guidance and leadership, they have received the commission's distinguished reports setting forth new principles and concepts, distilled from the shared thoughts of leaders in the many different fields that encompass the total problems of chronic illness. Seeking inspiration, they have found the unfailing enthusiasm and encouragement of the commission, its staff, its board, and its sponsors.

In short, we can agree that the commission has been the most powerful integrating influence at the national level in the field of chronic illness during the past seven years. They have been remarkable years—almost fabulous. Dynamic forces that brought the commission itself into being have accelerated during this period: the nation's expanding economy; our increasing and "aging" population; the trend toward urban and suburban life; and the ground swell of popular and professional interest in medical research, improved community health services, and care of the chronically ill. These forces are familiar to all of us, both in their general effects and in their specific dynamics. The role of the commission has been to channel some of these energies in new and constructive directions.

I believe that these new directions are more evident in the field of prevention than in any other major aspect of chronic illness, and I do not say this because progress in prevention is the only topic of my remarks. Evidence in support of my claim for progress in prevention of chronic illness is present on every hand—in the findings of laboratory, clinical, and epidemiological research and in the application of those findings in the offices of private physicians and in hospitals, clinics, and community programs.

I was fortunate in having a very useful series of documents to use as the basis for my comments. At the time of the commission's Conference on the Preventive Aspects of Chronic Disease in 1951, numerous voluntary health agencies, official organizations, and individual experts were asked to prepare summary statements on the major medical problems involved in the production of long-term illness. Recently, the commission asked the original authors if they would like to revise those statements before publication of the final report. The response was so enthusiastic that one could well accept the authors' desire to fit another chore into very busy schedules as evidence of significant progress in medicine and changes in approaches to health problems during the past five years.

I have selected for brief consideration at this time four concepts that appear in the statements that are now in the process of development. 1. Conscientious health workers can no longer make distinctions between preventive, curative, and restorative services for any type of illness, acute or chronic, infectious or noninfectious, local or systemic, degenerative, congenital, or what you will. We can call this unity of services. 2. The map of disease as we have known it is being remade constantly by medical explorers in as literal terms as the map of the world has been remade by the great geographers. 3. A new approach to personal health, particularly the health of children, is now possible and, perhaps, overdue. 4. A bolder willingness to incorporate medical and psychological methods for the prevention of chronic disease is needed in community programs, at the expense, if necessary, of traditional and less effective methods.

In elaborating these points, I would ask you to keep in mind that the revised statements have captured my attention more by their cross illumination than by the substance of individual texts alone. Crosslighting from one field penetrates another, or several, and seems to throw new light into some dark corners.

Surgeon General, U. S. Public Health Service, Department of Health, Education, and Welfare.

Read before the final meeting of the Commission on Chronic Illness, New York, Feb. 9, 1956.

Unity of Services

One of the new summary statements refers to restoration or rehabilitation as an attitude rather than as an exclusive body of medical techniques and recommends that all health personnel be oriented to this attitude. This strikes one as being a keenly perceptive idea that should be applied equally to prevention and cure. For the health professions have moved gradually toward unanimous consent that medicine is a whole fabric, a seamless robe, that cannot be cut into preventive, curative, and restorative parts and still retain its real utility.

Yet there has been little agreement on a modus vivendi in which health personnel now working exclusively in preventive, curative, or restorative programs can function as a whole body. In reading the new summary statements on chronic disease, we cannot escape the urgency of finding ways to work together. Many individuals, even whole groups, who are rendering health services today are operating under the illusion that their roles are exclusive. This is a hazardous position to cling to, for history and science are sweeping past that position to new heights.

Consider the following recommendations for the management of rheumatic fever and rheumatic heart disease:

> Patients with active rheumatic fever, as well as those with a history of rheumatic fever, should be under continuing medical supervision. The skills and knowledge of a wide variety of additional personnel are essential . . . physicians, nurses, medical social workers, occupational therapists, school teachers, and cooperative parents. . . . The patients may need the types of care provided by one or more facilities. . . . Special attention should be given to the protection of patients from exposure to group A hemolytic streptococcal infection. . . . Evidence indicates that the antibiotics used therapeutically in (such) infections will prevent subsequent rheumatic fever in the majority of cases.

Is the program preventive, curative, or restorative? It is none of these alone—but all three together. Medical research has provided bases for such unity of services. In the case of rheumatic heart disease, it has demonstrated relationships between streptococcic infections and rheumatic fever; it has discovered new drugs and demonstrated their value, not only in cure of streptococcic infections but also in prevention of rheumatic fever. The use of new drugs in the care of patients with or without infectious diseases has, in fact, altered some traditional concepts of prevention. I say concepts rather than practices, because, in too many instances, health agencies are still using traditional techniques that have little or no impact on the prevention of certain infectious diseases.

During the decade, 1945-1955, the domestic consumption of penicillin alone was nearly 3,000 tons, or 3 quadrillion units. In the same period, the death rates from streptococcic infections dropped 83%; from meningococcic meningitis, 95%; from acute rheumatic fever, 73%; from syphilis, 63%; and from pneumonia, 56%. These spectacular reductions in mortality were due not to prevention in the strict sense but to the vastly improved efficacy of therapeutic medicine. It can be said with considerable justification that the widespread use of antibiotics in medical and hospital practice actually has reduced the spread of many infections—whatever the specific conditions for which they were prescribed. More than ever before, every private physician, wittingly or unwittingly, had become a "health officer" in the old traditional sense of controlling communicable diseases.

The summary statements contain many recommendations that point to the need for unity of services. In some instances, such as in tuberculosis, the outlook for prevention in the strict sense is as hopeful today as it was in syphilis and its chronic complications five years ago. In others, such as the major degenerative diseases and congenital disorders, the road to prevention is still obscure, but it is certainly brighter than it was in 1951. At the present stage of medical knowledge, however, no type of prevention can be achieved in such conditions as cancer, many cardiovascular diseases, neurological disorders, metabolic diseases, and mental illness without full unity of services—preventive, curative, and restorative.

New Map of Diseases

No one who reads the statements can escape the impression that medical science is about to break through with a synthesis of recent findings that will establish new principles in our understanding of the human organism in disease and health. The map of disease is being made over. Here are a few excerpts from the statements:

> The clinical features of rheumatoid arthritis need to be redefined, because in recent years (a) the syndrome has been recognized as a disorder of the connective tissue system commonly having pluriorganic manifestations; (b) similarities and differences have been found in comparison with other obscure diseases of mesenchyma; (c) [there have been found] variants of both greater and lesser intensity than characterize the conventional clinical concepts of rheumatoid arthritis.

> The etiology of . . . essential hypertension is not known. It may well be compounded of various factors: renal, endocrine, nervous and cardiovascular. That this disease has a familial basis seems clear.

> Some of the causes or mechanisms involved [in multiple sclerosis] that have been proposed are: allergic tissue reactions in the central nervous system; localized or scattered vascular lesions due to vaso-constriction or to infections; alterations in the enzymatic support of myelin metabolism; dietary deficiency; exogenous intoxication; and specific emotional disturbance.

> At the present time, evidence seems to point to multiple causation of most emotional disorders. Hypotheses have been propounded to explain the development of emotional disorders on a psychological and social basis. Genetic factors have been implicated in some, such as schizophrenia.

> Knowledge of heredity and of the genetic mechanism involved [in epilepsy] can be extended by wider studies of family trees and of twin pairs. . . . Discovery of the physico-chemical process of the dysrhythmia which underlies seizures is as central to prevention as it is to treatment.

The theme of multiple causation runs through every one of these discussions and is as clear as though it had been printed in red ink. Among the prominent influences are genetic factors, stress reactions, metabolic and endocrine factors, and the interaction of the host—under various conditions and at different times of life—with a wide variety of exogenous agents, including viruses, poisons, drugs, and radioactive substances. The excellent discussions of heredity and nutrition summarize much of what is known or surmised about the multiple causation of chronic disease.

Is it not possible, then, that we are limiting our vision when we insist on the elucidation of specific etiology as a condition for prevention? Is it useful to attempt distinctions between primary and secondary prevention, any more than it has been useful to compartmentalize preventive, curative, and restorative services?

I throw out these questions because I do believe that we are much nearer the solution of many critical problems in chronic disease than we know. Our scientists on the outposts of medical reseach cannot limit their vision. If they could and did, we might as well abandon hope for the improvement of human health. An enormous amount remains to be learned, it is true, especially in the basic sciences related to human disease and health.

It is for these reasons that our Public Health Service request to Congress on the National Institutes of Health budget contains a 47% increase in funds for research grants-in-aid for 1957 over the funds we are spending for that purpose this year. That is why our research training budget requests are also much higher for next year. That is why we are increasing emphasis on basic research and why the President has asked for legislation to provide for grants-in-aid for construction of research facilities and for premedical teaching facilities.

Like the great geographers, our scientists, moving into the unknown, have given us good new maps in sector after sector of the chronic disease field. These guides make it possible for the health services to move forward and occupy new territory with a reasonable assurance of knowing that what they are doing has relevance to the control of the particular diseases. Only a few years ago, this was not true. Many practices were based on assumptions as incorrect as the early myths about two-headed people and fabulous monsters inhabiting the New World.

New Approaches to Personal Health

The clearing of the underbrush of empirical knowledge and "old wives' tales" is nowhere more apparent than in our concepts of personal health, particularly the health of children.

It is crystal clear in the summary statements that much of what we call chronic disease develops as the result of the total life experience, from the moment of conception onward. All of the insults and injuries, the deficiencies and stresses, arising from the environment and the biological inheritance, play a part. Sometimes, genetic influences originating many generations before are involved. Sometimes, the individual's adverse response to the challenge occurs early in life; sometimes it is a delayed reaction, perhaps precipitated by the processes of aging. Various parts of life experience may contribute different quantities to the development of disease or ill health.

At what point in the life experience, then, should we begin our efforts to prevent chronic disease? It seems equally clear that we should begin at a much earlier period than has been contemplated in most current health practices. All the evidence at hand indicates that serious long-term illness is destined to become increasingly a major threat to child health. Malignant disease is among the five leading causes of death among children from 1 to 15 years of age. Mortality rates from congenital malformations and heart disease are significant in the same age groups. The deaths of children from these causes, however, represent only a small fraction of the problem. Many children who survive the hazards of their prenatal life, birth, and early infancy are doomed to lifelong disablement as a result of mental retardation, cerebral palsy, other nervous disorders, blindness, and congenital defects. With our present high birth rate, we can expect to have increasing numbers of children at the risk of a greater amount of permanent disablement.

Increasing survivorship of infants who would have died without today's lifesaving measures may be related to an increase in cerebral palsy, although much of the cerebral palsy now occurring is preventable. The statement on cerebral palsy is a striking illustration of the need for new approaches to maternal and child health: "Rh incompatibility, for example, has declined as a cause of cerebral palsy from 10 percent to about 1 percent of the total cases, as a result of professional and public education, and the use of exchange transfusions." About 90% of the cases are accounted for by prenatal and natal causes, 60% occurring at birth. We would agree with the statement that "a more vigorous application of the various phases of the maternal health program, including better obstetric and neonatal care, may reap dividends."

Since more than 80% of all births in the United States occur in hospitals, we can also agree with the recommendation that the subject of cerebral palsy should be taught "as an integral part of the basic curriculum in medical schools and in schools for the training of the ancillary professions, rather than being reserved for postgraduate study." This orientation is needed as much to prevent the occurrence of cerebral palsy as it is to institute diagnosis and treatment early in life.

There are many new opportunities for the prevention of other chronic diseases in childhood and youth. More vigorous efforts to control accidents, for example, would not only save lives but would prevent much of the severe and permanent disablement that follows many nonfatal injuries. Each year, accidents permanently disable 10 times as many people as they kill. If the potentialities of early detection can be realized, it seems probable that a much larger number of cases of chronic disease in the earliest stages can be found in younger age groups. The statement on cancer supports that assumption.

The majority of cases of cancer and of many other degenerative diseases are first diagnosed in persons 45 years of age or older and are first diagnosed in moderately advanced and advanced stages. Yet in the recently developed program for the detection of cervical cancer, our experience shows that the earliest stages of the disease, when treatment is most effective, exist in larger proportions among younger persons than has been supposed heretofore.

Nearly 70% of the preinvasive cases of cervical cancer were detected in women under 40 years of age, with the surprising rate of 28% in the third decade, 20 to 29 years. In contrast, morbidity surveys show that only 22% of localized cervical cancers and only 15% of metastatic cases are diagnosed by conventional methods in women

under 40. On the average, an interval of about 15 years occurs between the development of intraepithelial tumors and the appearance of localized cervical cancer. There is time for prevention, indeed.

The advent of poliomyelitis vaccine points the way to removal of almost the last severely crippling infection from the long list that has threatened childhood and youth through the ages. The American population is going to be increasingly free of many diseases now concentrated in the first three or four decades of life. Medical research has given us some, and will give us more, techniques enabling the detection of the earliest stages of chronic disease. It has given us, and will give us more, effective techniques for treatment of all types, in a unity of services.

It would seem, then, that we should place more emphasis on the personal health of younger age groups. We should not relax our efforts for older people, but we should greatly intensify our efforts for the groups commonly thought to be the "healthiest," 15 to 34 years of age, for example. In those groups are the young parents and parents-to-be, who with the help of the health services can do the most to prevent long-term illness in children. In those groups are also the largest numbers of people who will be the long-term patients of tomorrow.

New Methods for Old

If the wealth of information in the summary statements is to be taken at full value, our community programs must develop new methods for the prevention of chronic disease. There must be a bolder willingness to incorporate the really thrilling new medical and psychological concepts into our approaches to prevention. In many instances, there must be a bolder willingness to face the facts of history and science and to agree that methods devised for disease control in the 1920's, for example, have little or no relevance to the people and the medical knowledge of the 50's. There are a few pacemakers vigorously applying new concepts in a few specialized agencies, a few hospitals, and a few community programs. The sum total is too small. The statement on emotional disorders and emotional factors in chronic disease is rich with forward-looking ideas and guides to some of the pacemaking programs.

There has been some bold facing of facts in the mental health field. It is demonstrated by the new movement to improve the care of mental patients in our public institutions. For that improvement to get started, the professions involved, the governors of states and their executive officers, and the public had to face the fact that, and I quote the statement, "some faulty methods of dealing with emotionally ill persons contribute to chronicity and disability." The Council of State Governments, the governors themselves, and their supporters have shown great courage in developing programs for the improvement of mental health along new lines. Some of the new methods being developed in mental health might well be applied to programs for other causes of long-term illness.

The important factor, however, is that the new methods spring from new attitudes—toward the problem, toward the scientific means now available, and, above all, toward the public and the patients of today. We need the fresh breeze of new attitudes in some of our health programs. Perhaps they would blow away the isolationism, uninspired routine, and defensiveness that characterize many of our services to our patients and the public. Here and there in the summary statements, these hampering attitudes are revealed—not by any light they generate but by the bright cross illumination from other sectors. They are revealed by the repetition of concepts that have been rendered worthless by scientific discovery and medical progress or by social progress, or by both. I shall not give you examples; if they remain in the statements, you will recognize them as warnings to keep always in touch with life—with the here and now of our changing society and the onward sweep of medical science.

Progress in the prevention of chronic disease during the life of the Commission on Chronic Illness has been greater than any of us could have foretold in 1949. It is the result of both those dynamic forces, social and scientific progress. People of the United States are better informed on health subjects; they enjoy a higher standard of living; they are better protected against serious illness and premature death from many causes; they receive better medical and hospital care; and more of them can pay for care. So equipped, our society will remain a powerful force to bring in a new era of greater freedom from long-term illness, whatever its cause.

Complete as the summary statements are, they contain only part of the tremendous progress in medical research and practice in these recent, fabulous years. We may look upon the findings as leading to prevention, cure, or restoration, as we choose. But this much is clear: Full application of only what is presented in the statements would so reduce the burden of chronic disease that the effects on the economic, social, and health status of the American people could be likened to the first great triumphs of preventive efforts against epidemic diseases. The commission has been a beacon lighting the way for many communities and organizations to undertake programs designed to speed that full application. May the lamps the commission has lighted never be extinguished.

Young Persons May Suffer Little Strokes.—Physicians must not forget that many young persons in their 20's and 30's suffer little strokes. . . . It takes courage to make the diagnosis of a little stroke in the case of a person in the early 30's. The same story in a person of 65 would excite no comment, and the diagnosis would not be questioned. What we must do is to remember the number of hemiplegic persons under the age of 30, whom we can see on any busy street in the course of a year. . . . A . . . patient, in his 30's, while waiting for breakfast, one Sunday morning, got a severe pain in his chest. When he telephoned for help, his doctor said he was at his office and could not leave for a time. The patient went to the doctor's building, and, because the elevator was not running, walked up two flights of stairs. The doctor made a diagnosis of heart attack; but I could not accept this, because the effort of going upstairs had not bothered him. It had neither added to his pain nor made him short of breath. Later, in the months that followed, his disability and distress were obviously not in his heart but in his brain; his electrocardiograms were normal. . . . This man, who had always been strong, well, uncomplaining, and a hard worker, on that Sunday morning had become a sad, uncomfortable, nervous person who could no longer earn a living. —W. C. Alvarez, M.D., More About Little Strokes, *Geriatrics*, December, 1955.

PERSISTENCE OF ABNORMAL HEPATIC TESTS IN CARRIERS OF VIRAL HEPATITIS

Robert F. Norris, M.D., Dicran Kassouny, M.D., John G. Reinhold, Ph.D.
and
John R. Neefe, M.D., Philadelphia

• *Fifteen recipients acquired viral hepatitis after a single blood transfusion. Tests for hepatic function—serum bilirubin, thymol turbidity, thymol flocculation, cephalin-cholesterol flocculation, zinc turbidity, urine urobilinogen, and sulfobromophthalein retention—had all given normal results in three of the donors.*

Twenty donors were examined repeatedly during periods up to four years after giving blood. One had consistently abnormal hepatic tests, yet his blood serum did not induce hepatitis in volunteers. Throughout the retesting period, each donor generally had consistently normal or abnormal results in the various tests. One donor developed clinical hepatitis seven months after donating blood that was believed to have caused hepatitis in a recipient and four and one-half months after his serum had caused hepatitis in volunteers; his blood still infected volunteers six months after his own clinical recovery.

At present the six tests enumerated are insufficient either to detect carriers with certainty or to pronounce a prospective donor safe.

It is a well-established fact that apparently healthy persons who volunteer to donate blood may be carriers of the hepatitis virus and that their bloods may be capable of transmitting the infection to recipients of blood transfusions.[1] Our previous report [1b] was concerned with the occurrence of viral hepatitis in 14 recipients of blood transfusions, a clinical evaluation of the 22 donors for these patients, and finally the demonstration of the carrier state in 5 donors. Of the 14 recipients, 8 received blood from only one donor, 4 from two donors, and 2 from three donors. At the time of examination, soon after the onset of viral hepatitis in their recipients, one donor for each recipient was reported to have at least one abnormal hepatic function test and was therefore suspected of being a carrier of the hepatitis virus. After inoculation of blood serum from six donors in separate groups of human volunteers, viral hepatitis occurred in one or more of the volunteers in five of the six groups. Meanwhile, a large group of blood donors was selected at random to determine the incidence of abnormal hepatic tests in a population of this sort.[2] The incidence was greater than we had expected. The test results in 12% of the donors were considered to be definitely abnormal and in an additional 17% were considered to be equivocal. When the results of the thymol turbidity test were considered alone, these figures were 6.6 and 9.1% respectively. How many of these abnormalities resulted from inapparent viral hepatitis is, of course, uncertain.

Unfortunately, a laboratory method is not now available for identifying the hepatitis virus in body tissues and fluids. If the hazard of transmitting viral hepatitis by transfusion is to be diminished before a specific diagnostic method is developed, search for another means of eliminating potentially infectious donors is important. Screening by means of hepatic function tests appears to be the only feasible method at the present time, but the rejection of all donors with abnormal hepatic tests would seriously handicap blood banking. The importance of increasing our knowledge about the relationship of abnormal hepatic tests to the carrier state of viral hepatitis therefore needs little emphasis. During the past four years we have repeatedly examined, by methods previously described,[3] the available donors for the 14 recipients who suffered from viral hepatitis. The results of this study are the subject of the present report.

Results of Study

The results of hepatic tests for the proved carriers and for the donors who were suspected but not proved to be carriers are tabulated separately in figures 1 and 2 respectively. Since the publication of our previous paper,[1b] a significant difference in the normal values of the zinc turbidity tests between whites and Negroes has been observed by Rawnsley, Yonan, and Reinhold.[4] Values in the present paper have been appropriately revised.

It is seen that donors 4 and 10b were examined only once. The 20 remaining donors were examined for periods up to four years from the time of the original donation. At least two hepatic tests were abnormal each time four of the proved carriers were examined. In the case of donor 2, the zinc turbidity measurement of 10.8 was at first considered equivocally abnormal, but, when the normal ranges were revised, this value became normal since the donor is a Negro. Although the sulfobromophthalein (Bromsulphalein) retention test was normal at the first examination, this test was positive whenever measured thereafter. In fact, retention gradually increased to a high value of 16% 684 days after donation.

Among the suspected carriers, donor 1 consistently had abnormal hepatic tests, although injection of his blood serum on one occasion did not induce viral hepatitis in volunteers. Donor 4, who was strongly suspected of being a carrier because he was the sole donor for his recipient and because three hepatic tests were abnormal, was not available for further observation. Donor 6, likewise a single donor for a recipient, had only a single equivocal test on two occasions and had all normal tests about a year after the donation. In the case of those recipients each having two donors, donors 9a and 9b both continued to show one or two abnormal hepatic tests,

From the William Pepper Laboratory of Clinical Medicine, University of Pennsylvania.

This investigation was sponsored by the Commission on Liver Disease of the Armed Forces Epidemiology Board and supported by the Office of the Surgeon General, Department of the Army.

for four years and two years, respectively, although on one occasion the former had all tests within the normal range. In this instance, both donors were suspected of having transmitted hepatitis to the recipient. Donor 10b, who was under suspicion at the time of the examination, would not return for further observation. In the case of donor 11a, also under suspicion, long-continued follow-up was prevented by his death in an automobile accident.

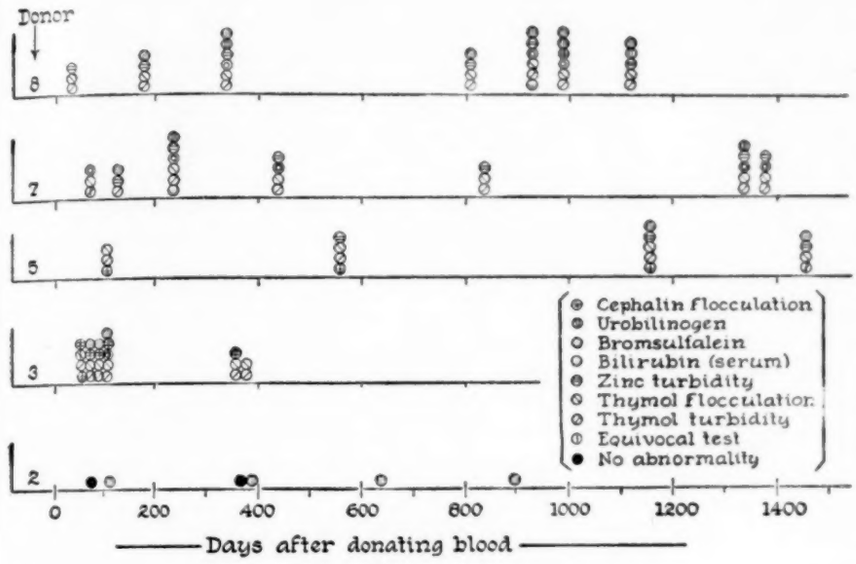


Fig. 1.—Results of hepatic tests for proved carriers.

Both donors 12a and 12b were tested at the time of donation and had one abnormal test each. When recalled at the time of onset of viral hepatitis in the recipient, donor 12b had hepatic tests that were normal and then remained so for the three-year period of observation, while donor 12a now had two abnormal hepatic tests and when tested nearly three years later still had one abnormal test. In the case of those recipients having received blood from three donors, donor 13c had only one equivocal hepatic test on one of two occasions shortly after the occurrence of viral hepatitis in his recipient, but, when he was tested again over three years after donation, two hepatic tests were abnormal. Donors 13a and 13b, on the other hand, were consistently normal. Donor 14c was a suspect in the case of the last recipient on the basis of one abnormal hepatic test, since donors 14a and 14b had normal tests at the time of onset of viral hepatitis in the recipient. These donors did not return for retesting until about three years after the donation. At this time each had a single abnormal hepatic test, but donor 14b had all normal tests when retested about a month thereafter.

Distribution of Abnormal Hepatic Tests.—The frequency distribution of abnormal hepatic tests is shown in the table. The donors are divided into three groups: those proved to be carriers; those suspected of being carriers because they were the sole donors for the recipients, because they had abnormal hepatic tests, or because of both; and those donors remaining. For each hepatic test, the percentage of abnormal measurements was calculated for each donor and the mean of the abnormal percentages was then determined for each group. It is seen that, in the case of the proved carriers, the percentage abnormal is much higher for each test than for the group of suspected donors. These data in general are another expression of those given in figures 1 and 2, which indicate that the proved carriers had a great number of abnormal hepatic tests at the time of first examination and that these tests showed a marked tendency to remain abnormal on subsequent testing. The data also show that the sulfobromophthalein retention, thymol turbidity, thymol flocculation, and zinc turbidity tests are, in the order given, the most frequently abnormal tests.

At the time each donor reported for laboratory tests, he was questioned concerning his health and was examined for the presence of hepatic disease. Donor 7 gave the most interesting history; this has been reported elsewhere,[1b] but it bears repetition here. The donor was admitted to another hospital with an attack of jaundice diagnosed as viral hepatitis beginning 209 days after the original donation and 74 days after the collection of blood serum that on inoculation induced viral hepatitis in volunteers. He was discharged from the hospital one month later. Although clinical evidence of hepatitis subsided, his liver continued to be palpable, and several hepatic tests were positive during the next few months (fig. 1). To determine whether his blood was still infectious, blood serum drawn on June 7, 1952, 444

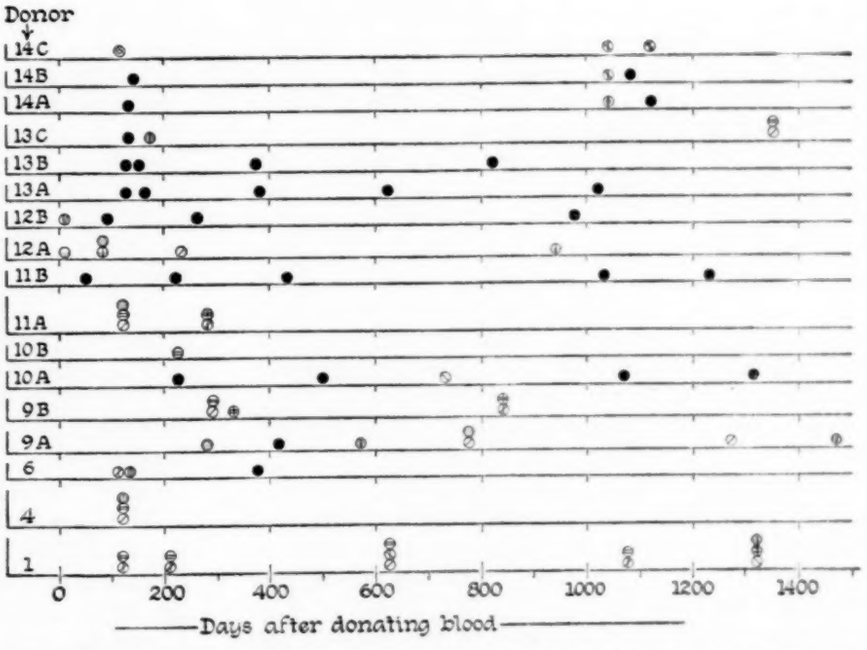


Fig. 2.—Results of hepatic tests for suspected carriers. (See figure 1 for explanation of symbols.)

days after the first donation and 204 days after discharge from the hospital, was injected into another group of volunteers by Murray and his associates.[5] Two of the five volunteers suffered attacks of viral hepatitis. In the two and one-half year period following this experiment, the donor has shown no objective changes in his physical condition, while hepatic tests have continued to give abnormal results.

Donor 8 was examined a number of times during a period of three years. Hepatic tests have been consistently abnormal (fig. 1), and the firm rounded liver edge has remained palpable about 5 cm. below the costal margin. Except for an occasional upper respiratory tract infection and a rare transitory gastrointestinal disturbance, the patient has remained asymptomatic. Donor 10a was exposed to his brother, who contracted a disease in May, 1954, that was diagnosed as viral hepatitis. The donor remained asymptomatic. Donor 14a had a cholecystectomy at another hospital for biliary colic and has been well since the operation. At the time of last examination, the liver was just palpable in the case of donors 14b and 14c. The remaining donors have had no symptoms or physical findings suggesting the presence or continuance of hepatic disease.

Percentages of Abnormal Hepatic Tests

Hepatic Tests	Proved Carriers (5)	Suspected Donors with Abnormal Tests (10)	Other Donors (7)
Serum bilirubin	19	3	0
Thymol turbidity pH 7.55	80	47	0
Thymol flocculation pH 7.55	77	9	8
Cephalin-cholesterol flocculation	25	5	7
Zinc turbidity	70	53	0
Urine urobilinogen	38	5	5
Sulfobromophthalein retention	84	43	0

Comment

The data indicate that hepatic tests for both the proved and suspected carriers tend to give consistent results over a long period of time whether normal or abnormal in varying degree (fig. 1 and 2). Since abnormal hepatic tests persisted for several years in four of five proved carriers, these donors would have been continually rejected by a screening program that includes the thymol turbidity and flocculation tests. Whether the carrier state has continued for a similar length of time is of course unknown. Donor 1, who is still suspected of being a carrier, although on one occasion his blood serum did not induce viral hepatitis in 10 human volunteers, would also have been repeatedly rejected as a donor. The suspected carriers 4 and 11a might also have been rejected as donors over a long period of time, but the data are insufficient to establish this point. Nine of the remaining donors would have been rejected on every occasion examined on the basis of these two tests alone.

It is unfortunate that the sulfobromophthalein retention test is not suitable for screening purposes. Each time retention was measured after the initial examination in the proved carrier, donor 2, the result was significantly abnormal. On the other hand, the fact should again be emphasized that concentrations of serum bilirubin and urine urobilinogen were seldom increased above normal in the proved carriers and that increased bilirubin in urine could not be demonstrated at any time in any of the carriers except during the period of frank jaundice of donor 7.

At the beginning of our study of donors suspected of being carriers of the hepatitis virus, the donors selected for transmission experiments in human volunteers had been the sole donors for their recipients and had had one or more abnormal hepatic tests. When it was demonstrated by means of transmission experiments in human volunteers that five of six donors were actually carriers of the hepatitis virus, it was the plan to duplicate these experiments with blood from suspected carriers showing no evidence of hepatic disease in order to ascertain whether the carrier state can also be demonstrated in persons having normal hepatic tests. We were unable to conduct this experiment because human volunteers were no longer available for this purpose. Meanwhile, a proved carrier with repeatedly normal hepatic tests was reported by Stokes and associates.[1a] None of the single donors for recipients (donors 1 through 8) in the present study, however, repeatedly had all tests within the normal range.

During the past two years, four additional cases of viral hepatitis following a single transfusion have come to our attention. The donors in all the cases were first examined after viral hepatitis was diagnosed in the recipients. The hepatic tests of one gave all normal results; those of a second gave normal measurements except for an equivocal sulfobromophthalein retention test; those of a third gave a positive thymol turbidity test that gradually became normal in a period of eight months; and those of the fourth donor, who was examined only once, gave positive thymol turbidity and flocculation tests and a positive sulfobromophthalein retention test. There are indications, therefore, that some persons carrying the hepatitis virus in their blood will have repeatedly normal hepatic tests. If these single donors who are either proved or suspected carriers are taken together with those of Stokes and associates,[1a] it is seen that only 3 of 15 had entirely normal hepatic tests at the time of the first examination after the occurrence of viral hepatitis in the recipients, and one of them (donor 2) thereafter had repeatedly abnormal sulfobromophthalein retention tests. If the thymol turbidity and flocculation tests alone are considered, 4 of 15 gave normal results.

For comparison we have recently published figures that show that about 70% of blood donors have all normal hepatic tests and 84% show normal thymol turbidity and flocculation tests.[2] The data accumulated so far, however, are insufficient to determine the relative proportions of carriers showing abnormalities of hepatic tests as compared with those showing no abnormalities of these tests. If the number of the latter is large as compared with the number of carriers having abnormal hepatic tests, the effectiveness of a screening regimen based on these tests will be correspondingly reduced.

There are indications that persons suffering from clinically apparent viral hepatitis may be carriers of the virus in their bloods during convalescence.[6] It has been suggested, however, that blood from such individuals should be acceptable for use in transfusion when the patient has recovered completely, because antibodies

against viral hepatitis should be present after recovery. According to this view, convalescent blood should actually confer passive immunity on the recipient against the hepatitis virus in other potentially infectious bloods. Following this line of reasoning, blood from donor 7 was again inoculated into human volunteers more than six months after the donor's convalescence from an attack of viral hepatitis. The occurrence of viral hepatitis in two of the five volunteers does not support the assumption that blood from such persons can be regarded as acceptable for transfusion. It should be emphasized, however, that hepatic tests of this donor were continually abnormal during and after convalescence. In the case cited, the attack of jaundice may have been an exacerbation of a latent viral infection that then subsided into a state of clinical dormancy. On the other hand, the donor may have recovered from infection with one strain of hepatitis virus only to acquire an infection with a second strain. So far as could be determined, none of the donors other than donor 7 suffered from an attack of viral hepatitis during the periods of observation.

Summary and Conclusions

Twenty-two donors for 14 recipients who suffered from viral hepatitis after transfusion were recalled repeatedly for clinical examination and hepatic tests. Five of the donors had previously been shown to be blood carriers of the hepatitis virus. The results of hepatic tests in the proved carriers and in the remaining donors did not vary greatly in any case for periods of as long as four years. All of the proved carriers consistently had one or more hepatic tests abnormal while under observation. Four of the five proved carriers would have been repeatedly rejected as blood donors solely on the basis of the thymol turbidity and thymol flocculation tests with the reagent buffered at pH 7.55.

Evidence is presented that indicates that some carriers may have repeatedly normal hepatic tests. Fifteen recipients acquired viral hepatitis after a single blood transfusion or after transfusion from a subsequently proved carrier; three donors for these patients had all normal hepatic tests when first examined. Since only 4 of the 15 donors showed normal thymol turbidity and thymol flocculation tests, 11 of them presumably would have been rejected as donors if these tests had been employed as a screening procedure. The proportion of carriers having normal tests to those having abnormal hepatic tests is not yet known. One carrier suffered from clinical viral hepatitis seven months after donating the blood that is presumed to have caused viral hepatitis in the recipient and four and one-half months after inoculation of his blood serum caused viral hepatitis in human volunteers. The serum of this carrier was also infectious for volunteers six months after clinical recovery from viral hepatitis. None of the other donors in this group suffered from overt attacks of viral hepatitis during the period of observation.

1. (*a*) Stokes, J., Jr., and others: The Carrier State in Viral Hepatitis, J. A. M. A. **154**: 1059-1065 (March 27) 1954. (*b*) Neefe, J. R., and others: Carriers of Hepatitis Virus in the Blood and Viral Hepatitis in Whole Blood Recipients, ibid. **154**: 1066-1074 (March 27) 1954.

2. Fitch, D. R., and others: Incidence of Latent Hepatic Disease in Blood Donors: Possible Relation to Carrier State of Viral Hepatitis, Am. J. Clin. Path. **25**: 158-165 (Feb.) 1955.

3. Footnote 1*b*. Reinhold, J. G.: Chemical Evaluations of the Functions of the Liver, Part 1, Clin. Chemist **5**: 82-88 (Dec.) 1953; part II, ibid. **6**: 3-10 (Feb.) 1954; part III, ibid. **6**: 21-27 (April) 1954; part IV, Clin. Chem. **1**: 351-421 (Dec.) 1955.

4. Rawnsley, H. M.; Yonan, V., and Reinhold, J. G.: Protein Concentrations in North American Negro, Science, to be published.

5. Murray, R., and others: To be published.

6. Havens, W. P., Jr.: Infectious Hepatitis, Medicine **27**: 279-326 (Sept.) 1948. Neefe, J. R.: Viral Hepatitis: Problems and Progress, Ann. Int. Med. **31**: 857-870 (Nov.) 1949.

AGED IN CONNECTICUT STATE MENTAL HOSPITALS

STUDY OF PERSONS OVER SIXTY YEARS OF AGE AT THREE CONNECTICUT STATE MENTAL HOSPITALS

Sidney Shindell, M.D.
and
Elizabeth Cornfield, M.D., Rocky Hill, Conn.

• Crowding in mental hospitals has at times been ascribed to a supposedly large number of senile patients who do not really need the safeguards and facilities of psychiatric care and could be transferred to other institutions for the aged or the chronically ill. This survey concerns patients over 60 in three state mental hospitals.

A representative sample from each hospital was studied in sufficient detail to determine whether each patient satisfied certain criteria, so as to eliminate the suicidal, the negativistic, the destructive, the assaultive, the disoriented, and so on. Of the 10,289 patients carried on the census of these hospitals, there were 4,178 over the age of 60. Of these, only 231 in this study could be considered able to be transferred.

Since November, 1954, the Commission on the Care and Treatment of the Chronically Ill, Aged, and Infirm, in cooperation with the Connecticut Department of Mental Health, has been carrying on a program to transfer a significant number of elderly patients from the state's three mental hospitals (Connecticut State Hospital, Middletown; Norwich State Hospital, Norwich; and Fairfield State Hospital, Newton) to a newly opened chronic illness facility. This program has presented an opportunity to determine the extent to which care outside a mental hospital is feasible for these elderly patients.

Previous Studies on the Aged in Connecticut

Several reports have been published in Connecticut, during the past 15 years, containing conflicting estimates of the problem under study. In 1940, the report of the

From the Commission on the Care and Treatment of the Chronically Ill, Aged, and Infirm.

Read before a joint meeting of the Commission of the Mental Health Council, New Haven, Conn., March 10, 1955.

Commission on the Treatment and Care of People Afflicted with Physical or Mental Disabilities was published. It stated: "There are many hundreds of persons, mostly aged, who are now patients in the hospitals for the insane who do not require the specialized psychiatric care provided by such hospitals." [1] The report of the Public Welfare Council, prepared in 1944 for the 1945 general assembly, indicated that "a careful case analysis of patients at the Norwich State Hospital in February, 1944, revealed that 225 patients were eligible for removal under . . . the Sanitary Code." [2] Projecting this figure to the other mental hospitals, the report further stated: "Thus there would be at least 620 such patients needing infirmary care." In 1950, a committee of three physicians was requested by the Commission on the Care and Treatment of the Chronically Ill, Aged, and Infirm to survey all three mental hospitals to develop an estimate of the number of patients in state mental hospitals suitable for care with essentially normal elderly people. They arrived at a figure of 300 people who "for the most part are capable of a reasonable degree of self-care and of profiting from occupational, social and recreational activity of a type suitable for essentially normal elderly people." [3]

All of the above shared two deficiencies. On one hand, they were with one exception simply estimates and were not supported by statistically adequate data. On the other, they were not supported by experience with actual transfers to validate the accuracy of the estimates. The former joint committee of the state mental hospitals, and the department of mental health that superseded it, have repeatedly emphasized the fact that persons 60 years of age and over represent one-third of the admissions to the mental hospitals. This fact, coupled with statements reiterating in part the results of former surveys and estimates, has helped to create the widely disseminated impression that a substantial portion of the aged in the mental hospitals "don't belong there."

Present Study

In an attempt to provide data that would survive the closest scrutiny and to present as accurate a definition and assessment of the problem as possible, the Commission on the Care and Treatment of the Chronically Ill, Aged, and Infirm, while transferring cases for care at its Undercliff Hospital, conducted the study reported in detail below.

Who Are the Aged Now in Connecticut State Mental Hospitals?—As of specific dates, the total census of each of the three mental hospitals was determined. The age of all patients included in each census was then noted, and separate alphabetical listings were prepared of the males and females who were, on the date of each census, at each of the three mental hospitals. By a table of random numbers [4] a 10% sample was obtained from each of the six such lists. Table 1 shows the number of persons carried on the mental hospitals' census, the number 60 and over, and the number included in the survey sample. Table 2 shows the diagnoses as recorded by the mental hospital staffs on the survey patients. It can readily be seen from this table that the major portion of the older persons residing in the mental hospitals cannot be considered simply problems of senility, or of circulatory disease of the brain accompanying old age, since these groups account for only 36% of the patients. Similarly, when analyzing the age of the patients on admission to the mental institutions, one finds that a large number of elderly persons now in the mental hospitals have grown old in the institutions. Table 3 shows the age of the 60-year-old and over survey patients on their last admissions to the mental hospitals. It does not include the time spent in mental hospitals on prior admissions, which is substantial in many instances. From this table it can be seen that less than half (47.2%) the individuals were 60 years of age or older when admitted to the mental hospitals. Further breakdown of the group 60-69 shows that actually only 36.7% of the survey group was 65 or over when admitted. It is obvious, therefore, that the aged in the mental hospitals constitute two groups: (1) those who grew old while under care in the mental hospitals, and (2) those who were admitted during their later years.

Who of the Aged in the Mental Hospitals Can Be Transferred?—Admittedly, the most difficult phase of the study was the development of suitable objective criteria to be applied to each patient (see figure). Prior to

TABLE 1.—*Census of Mental Hospital Patients Aged Sixty and over and Survey Samples, by Sex**

	Total			Connecticut State Hospital, Oct. 23, 1954			Norwich State Hospital, Nov. 11, 1954			Fairfield State Hospital, Dec. 4, 1954		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Census												
All patients	10,289	4,662	5,627	3,480	1,561	1,919	3,583	1,653	1,930	3,226	1,448	1,778
Patients aged 60 and over	4,178	1,747	2,431	1,451	595	856	1,424	606	818	1,303	546	757
% of total census	40.6	37.5	43.2	41.7	38.1	44.6	39.7	36.7	42.4	40.4	37.7	42.6
Survey sample												
10% of patients aged 60 and over	417	174	243	145	59	86	141	60	81	131	55	76

* These figures include all persons counted by mental hospitals as patients and includes all those on extended visit either at home or under special arrangement in selected nursing homes.

TABLE 2.—*Primary Diagnoses* of Patients in Survey Sample*

Diagnoses	No. of Patients	%
All diagnoses	417	100.0
Organic brain disease associated with aging	150	36.0
Cerebral arteriosclerosis and other circulatory disturbances	110	26.4
Senile brain syndrome	40	9.6
Other acute or chronic brain syndromes	34	8.2
Functional psychosis	212	50.8
Schizophrenia	154	36.9
Other (involutional, manic-depressive, paranoid reactions)	58	13.9
Miscellaneous (mental deficiency, personality disorders, neuroses, and no diagnosis)	21	5.0

* Diagnoses are those reported by the mental hospital staffs.

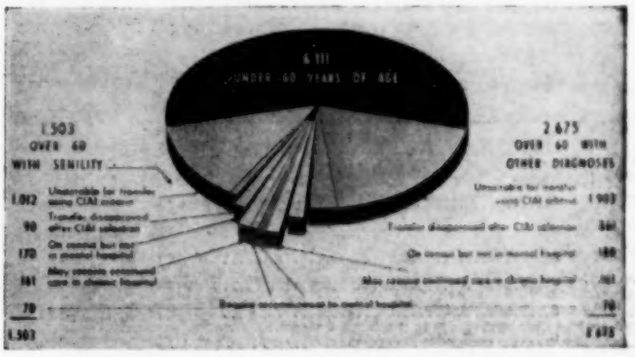
the selection of the random sample for the study, the cases of 198 patients chosen by one of the mental hospitals for possible transfer were reviewed. In this group, 178 patients showed behavior problems that seemed to indicate need for their continued care in a mental facility. These behavior problems were classified and used as the criteria for selection of the patients included in the study. Each patient in the study sample, regardless of diagnosis and age on admission, was evaluated for transfer to the Undercliff Hospital. The charts on all of the survey patients were reviewed, the staff members who cared for the patients at the mental hospitals were interviewed, and the patients themselves were seen in most instances. One physician investigator, acting as a recorder of available information, did the entire project, so that the data obtained in each of the three mental hospitals can be considered comparable.

A brief explanation of the criteria seems in order. The basic premise was that, in order for a patient to be suitable for removal from a mental hospital, the manifestations of his mental illness must be such that they constitute no danger either to himself or to other patients. Further, his behavior could not be so socially unacceptable or disturbing as to interfere with adequate care for other patients. Essentially, the criteria used were based on the premise that a patient with any significant aberrant behavior should remain within the confines of a mental institution. Traditionally the mental hospital system has served the function of separating from society individuals who demonstrate significant abnormal behavior. The difficulty in specific instances is one of defining how abnormal such behavior must be to justify such separation.

TABLE 3.—*Age of Patients (Now over Age Sixty) at Time of Most Recent Admission to Mental Hospital*

Age, Yr.	No. of Patients	%	Male	Female
All ages	417	100.0	174	243
Under 30	25	6.0	14	11
30-39	58	14.0	27	31
40-49	64	15.3	23	41
50-59	74	17.7	26	48
60-69	89	21.4	40	49
70-79	71	17.0	35	36
80 and over	36	8.6	9	27

Recognizing that terms such as "confused," "disturbed," or "psychotic" were too nonspecific to apply as criteria, the following questions served to specify the aspects of behavior that would militate against care outside a mental institution. 1. Have suicide precautions been found necessary or advisable by the mental hospital in the management of this patient? 2. Is there evidence of deliberate attempts on the part of the patient to escape from the institution? 3. Is the patient assaultive or destructive? It is obvious that affirmative answers to any of these questions would make it impossible to care for the patient in an institution having no security measures. 4. Is the patient abusive to other patients or staff members, or does he use profanity that is unduly disturbing? 5. Is the patient more than occasionally noisy to the extent of creating disturbances among other patients? 6. Is the patient untidy with excreta, as opposed to incontinence? These questions give indications of behavior that is extremely distressing and upsetting (rather than actually dangerous) to other patients and that is frequently the type of antisocial behavior that prompted the present admission to mental hospital. In addition to the above features, the following questions were also considered. 7. Can the patient understand simple instructions? 8. Can he communicate his basic needs? 9. Is he resistive to the routines of a hospital, such as taking medicaments, taking baths, and keeping covered with bedclothes?



Results of survey to determine which elderly patients in mental hospitals could be transferred to a chronic illness facility. There were 10,289 patients (all ages) in Connecticut state mental hospitals during the winter of 1954.

Patients were considered unacceptable because of inappropriate answers to these questions only if the basis for these answers lay in mental illness or deficiency. For example, deafness or aphasia preventing communication was not considered disqualifying, whereas a complete withdrawal such as is exhibited by a catatonic state was considered disqualifying. Any miscellaneous observations were also noted. When manifestations of unsuitable behavior that were not included in the above questions were encountered, they were noted as "Remarks" on the individual case records. The vast majority of these findings were obvious symptoms of frank mental illness, such as delusions, hallucinations, and hyperactivity. In no case was severity of physical illness a factor in selection, and all degrees of disability were accepted including paralyses, incontinence, blindness, decubitus, and neoplasms. Patients with severe physical illness coupled with aberrant behavior were considered on the same basis as ambulatory patients with aberrant behavior.

TABLE 4.—*Number of Patients Having Disqualifying Responses to Specific Criteria Applied*

Criteria	No. of Patients
Suicide risks	12
Escape risks	16
Assaultive or destructive	117
Abusive or profane	96
Untidy, noisy, or disturbing	135
Untidy with food or excreta	97
Impaired comprehension	138
Impaired communication	146
Resistive to hospital routine	132
Miscellaneous	104
Total patients	291
Total disqualifying responses	992
Mean no. of responses per patient	3.41

Table 4 shows the number of patients demonstrating behavior that was considered disqualifying, as reflected by each of the criteria applied. Table 5 shows the num-

ber of disqualifying responses of all categories per patient for those deemed unsuitable for transfer. It can be seen from these tables that there was significant evidence of disqualifying behavior in all the patients evaluated. A mean of 3.41 disqualifying responses per patient was obtained for the entire series, with the patients who may

TABLE 5.—*Number of Disqualifying Responses per Patient, by Diagnostic Groupings*

No. of Responses	No. of Patients with CBS Due to CAS or SBD *	All Others
1	16	36
2	12	35
3	20	42
4	16	32
5	22	18
6	12	15
7	3	11
8	0	1
Total patients	101	190
Mean no. of responses per patient	3.63	3.29

* CAS = cerebral arteriosclerosis and SBD = senile brain disease. The two are grouped together as "seniles." CBS = chronic brain syndrome.

loosely be termed "senile" accounting for slightly more per patient than all others. Table 6 shows the number of persons the investigator felt were acceptable for transfer after applying these criteria. No data were obtained to account for the difference between the sexes reflected in this table.

The acceptance by the investigator of a specific patient was followed by a reevaluation of the patient's status at the mental hospital. Those who were included in the census although actually at home or in nursing homes under supervised visit were retained on that status. Those for whom the family refused to consent to transfer were similarly withheld. In a significant number of instances the mental hospital staff felt that the psychiatric prognosis was too poor to risk discharge from the mental hospital. Table 7 shows the disposition of all cases, by mental hospital, deemed suitable by the investigator for transfer. Table 8 shows similar data by diagnostic grouping. From these tables it may be seen that of the significant number of aged persons who met the criteria for transfer, the major portion were not available for transfer. No data are available to account for the difference among the

TABLE 6.—*Number and Percentage of Patients in Survey Sample Deemed Acceptable by Investigator for Transfer*

	No. of Patients		
	Total	Male	Female
Total survey sample	417	174	243
Acceptable to Commission on Care and Treatment of Chronically Ill, Aged, and Infirm	126	71	55
% of patients 60 and over in sample acceptable	30.2	40.8	22.6

three mental hospitals. It does not appear that the criteria employed were too strict. Evidence of this is found in the fact that patients whose cases met the criteria had to be returned to the mental hospital after transfer to the chronic hospital. Further, the mental hospitals themselves withheld apparently acceptable cases as unsuitable in their judgment.

Comment

It may then be concluded, from projecting the above survey data to the total group of patients over 60 in the mental hospitals, that the expected number of individuals who are able to be cared for in other types of facilities equals an extremely small number of the entire group over 60. Specifically, of the 4,178 persons aged 60 and over in the three mental hospitals, 1,263 may be expected to meet the criteria for transfer. Only 491 of these can reasonably be termed "seniles." Of these so-called seniles 231 are to be expected to be available for transfer to chronic facilities, since 90 were either subsequently deemed unsuitable for transfer by the mental hospitals or refused transfer and 170 had already had arrangements made for care outside the mental hospital,

TABLE 7.—*Disposition of Survey Patient Acceptable to Investigator for Transfer, by Mental Hospital*

Disposition	Total	Connecticut State Hospital	Norwich State Hospital	Fairfield State Hospital
Patients acceptable to Commission on Care & Treatment of Chronically Ill, Aged, and Infirm	126	54	40	32
Retained on census by mental hospital	75	17	33	25
Unsuitable for transfer *	42	6	14	22
Patient's family refused transfer	3	0	1	2
"On visit" or in convalescent home	30	11	18	1
Died or discharged	5	3	1	1
Available for transfer	46	34	6	6

* This determination made by the mental hospital after selection by above criteria.

TABLE 8.—*Disposition of Survey Patients by Diagnostic Grouping*

Disposition	Total	CAS and SBD *	All Others
All survey	417	150	267
Acceptable to Commission on Care and Treatment of Chronically Ill, Aged, and Infirm	126	49	77
Not available for transfer	80	26	54
Unsuited or refused	45	9	36
Already out	35	17	18
Available for transfer	46	23	23
% of survey available for transfer	11.0	15.3	8.6

* CAS = cerebral arteriosclerosis and SBD = senile brain disease. The two are grouped together as "seniles."

even though they are carried on the mental hospital census. In addition to the "seniles" there were found to be 772 persons, admitted originally for diagnoses other than senility, who seemed to meet the criteria for transfer; however, of these only 231 could be considered able to be transferred, since 180 had arrangements for extra-hospital placements and the remainder were considered by the mental hospital as unsuitable for transfer.

At best, therefore, there were 462 individuals at the time of the survey who could conceivably be removed from the state mental hospitals. After transfer to chronic facilities, many of these people show unsuitable behavior sufficient to warrant their return to a mental hospital setting. The precise number of these individuals is not yet available, but preliminary experience indicates that probably 70 of each group cannot make a continued adjustment outside mental hospital walls, leaving but 322 in-

dividuals who at the time of the survey could be cared for in chronic facilities. The Commission on the Care and Treatment of the Chronically Ill, Aged, and Infirm, in the four months since the survey was begun, has already undertaken to care for about 200 such individuals. The evidence reported above indicates that, at least in Connecticut, the "seniles" who can be cared for outside mental hospitals have not contributed to a substantial degree to crowding in mental hospitals and that efforts undertaken by both the mental health department in its boarding-out program and the Commission on the Care and Treatment of the Chronically Ill, Aged, and Infirm have now removed the substantial majority of such cases from the mental hospitals.

Summary

A 10% random sample of patients 60 years of age and older in the three Connecticut state mental hospitals was studied by a set of criteria used to reflect dangerous or antisocial behavior to determine the feasibility of transferring such patients to chronic illness facilities. On the basis of this survey the following conclusions have been drawn. 1. The number of aged in mental hospitals who can be cared for elsewhere is a small percentage of the mental hospital population (6.5%), of which over half (3.5% of total) have already been removed, although carried on the mental hospital census. 2. The number of aged loosely termed "seniles" who may be cared for elsewhere is only 1.5% of the total mental hospital population. The data appear to indicate that the use of chronic facilities to care for aged persons who have been admitted to mental hospitals represents simply one method that may be used in providing appropriate care to persons who are in the normal discharge channels of the mental hospital system.

West Street (Dr. Shindell).

1. The Commission on the Treatment and Care of People Afflicted with Physical or Mental Disabilities: Report, Hartford, Conn., 1940, p. 11.

2. The Public Welfare Council: Need for a State Infirmary for the Care and Treatment of Aged, Infirm and Chronically Ill Persons, A Report to the 1945 General Assembly, Hartford, Conn., 1944, p. 40.

3. Silbermann, S. J.; Solomon, C. I., and White, B. V.: Survey of Patients in State Mental Hospitals Suitable for Care with Essentially Normal Elderly People, 1950, p. 2.

4. Arkin, H., and Colton, R. R.: Tables for Statisticians, College Outline Series, New York, Barnes & Noble, Inc., 1953, table 23, pp. 142-145.

INTERMITTENT POSITIVE-PRESSURE BREATHING

APPRAISAL OF USE IN BRONCHODILATOR THERAPY OF PULMONARY EMPHYSEMA

Alan Leslie, M.D., D. Alfred Dantes, M.D.
and
Leon Rosove, M.D., Los Angeles

• *Thirty-three patients with pulmonary emphysema and various degrees of bronchospasm, fibrosis, bronchiectasis, and chronic infection were treated with bronchodilator drugs, with and without intermittent positive-pressure breathing. The three bronchodilators used were power-nebulized for inhalation and were given in random sequence so as to determine which was most effective for each patient. The apparatus used for the positive-pressure breathing was set for a pressure of 15 to 20 cm. H_2O.*

In the first phase of the study, each drug was used four times for each patient, twice with and twice without pressure breathing. Quantitative data on vital capacity were obtained. The improvement seen when the bronchodilators were used alone was not significantly enhanced by the pressure breathing.

In later phases of the study, the treatments were given over longer periods of time, again with and without pressure breathing. Evidence of the effectiveness of the bronchodilators and the advantages of power nebulization was obtained, but the benefits did not appear to be enhanced by intermittent positive-pressure breathing.

Patients with the disease triad of chronic pulmonary infection, fibrosis, and emphysema usually follow an inexorable downhill course. Until recently the available therapy was relatively ineffective. It consisted of bronchodilator agents, potassium iodide, postural drainage, and so-called breathing exercises, sometimes supplemented by abdominal binders or pneumoperitoneum. "Climatotherapy" in the management of this disease was a rationalization used in order to justify sending problem patients to distant places. This usually contributed more to the physician's peace of mind than it did to the patient's health.

The basic objectives of therapy of this type of pulmonary disease are the control and prevention of infection and bronchospasm. With the application of newer therapeutic methods, the attainment of these objectives seems less remote. Thus, the prognosis, although still grim, is somewhat improved. The progressive pulmonary damage attendant upon recurrent or chronic lung infection now can be held at least partially in abeyance by the use of antibiotics and a more effective bronchodilator therapy, in addition to the usual less specific measures.

Bronchodilator medicaments may be administered orally or rectally, by injection, and, probably most effectively, by inhalation. Hand nebulizers have the advantage of portability but deliver relatively small quantities of drug for inhalation. For the delivery of larger quantities of drug it is desirable to use an external source of power for nebulization. This may be an air compressor, or, more conveniently, a cylinder of compressed air or oxygen that provides a continuous controllable flow through the nebulizer.

From the Medical Service, Veterans Administration Center, and the Department of Medicine, University of California Medical Center.

The oxyphenonium bromide used in this study was supplied as Antrenyl by Ciba Pharmaceutical Products, Inc., Summit, N. J.

The value of combining intermittent positive-pressure breathing with the power nebulization of bronchodilator drugs has been under investigation.[1] Beneficial results of this combined therapy have been uniformly reported. Fowler, Helmholz, and Miller [1d] made the pertinent observation that the practice of combining several therapeutic measures (oxygen, intermittent positive-pressure breathing, and bronchodilators) makes the assessment of their individual merits very difficult. In order to evaluate the role of intermittent positive-pressure breathing, these investigators therefore compared the effects of oxygen power nebulization of a bronchodilator administered with intermittent positive-pressure breathing to the results obtained by nebulization of the same bronchodilator without the use of intermittent positive-pressure breathing. They observed approximately the same degree of benefit after both procedures. Because of the question thus raised concerning the benefits deriving specifically from the intermittent positive-pressure breathing component of the combined therapy, it was decided to undertake further studies over a longer period in an attempt to elucidate the problem.

Procedure

Thirty-three patients with moderate to advanced pulmonary emphysema associated with various degrees of bronchospasm, fibrosis, bronchiectasis, and chronic bronchopulmonary infection were studied. The diagnoses were made by history, physical examination, roentgenography, and ventilometry. The investigation was performed in three parts.

The first part was designed for two purposes: (1) to determine the immediate effects of various power-nebulized bronchodilators administered alone and combined with intermittent positive-pressure breathing, and (2) to determine for each patient which of the bronchodilators administered was most effective. The three drugs used and their dosages were: isoproterenol (Isuprel) hydrochloride, solution 1:200, 0.5 ml.; cyclopentamine hydrochloride and isoproterenol hydrochloride (Aerolone) compound, solution no. 50, 0.5 ml.; and oxyphenonium (Antrenyl) bromide, 2 mg. Each of these drugs was diluted with distilled water to a volume of 1 ml. and nebulized by a continuous flow of oxygen. The rate of flow, about 4 liters per minute, provided complete nebulization of the drugs over the 20-minute period of administration. These drugs were given separately, in random sequence, to each patient on 12 days. On six of these days the drugs were administered by means of a nebulizer let into the face of a BLB oronasal mask with respiration proceeding at atmospheric pressure. On the other six days the drugs were administered by means of a Bennett pressure breathing therapy unit, model TV-2P, a valve-mask–nebulizer–intermittent positive-pressure breathing apparatus, set at a pressure of 15 to 20 cm. H_2O. Thus, each drug was used four times for each patient, twice with and twice without added intermittent positive-pressure breathing. Observations of the volume of deep respiration, inspiratory and expiratory vital capacities, and E–E′ difference expressed in per cent of the inspiratory vital capacity (E represents maximum exhalation immediately after quiet breathing; E′, the maximum exhalation after the initial maximum exhalation and a maximum inhalation [2]) were made before each treatment and again 10 minutes after each treatment.

The second part of the investigation, a period of four weeks, was designed to compare the results of short-term therapy with an oxygen-nebulized bronchodilator alone to those of a comparable period of treatment with the oxygen-nebulized bronchodilator plus intermittent positive-pressure breathing. The most effective bronchodilator for each patient, as determined in the first part of our investigation, was used in each case. Cyclopentamine hydrochloride and isoproterenol hydrochloride compound solution was used in the treatment of 10 patients; isoproterenol hydrochloride solution in that of 11; and oxyphenonium bromide in that of 12. Twenty patients received treatment without intermittent positive-pressure breathing twice daily for two weeks. For the second two weeks they received identical treatments, but with intermittent positive-pressure breathing also. Thirteen other patients were similarly treated, except that intermittent positive-pressure breathing was added during the first two week period but not during the second. Observations of volume of deep respiration, inspiratory and expiratory vital capacities, and E–E′ percentage were made on the first day of the four week period, after two weeks, and after four weeks.

The third part of the investigation was planned to evaluate the results of an extended period of combined bronchodilator–intermittent positive-pressure breathing therapy. Isoproterenol hydrochloride solution, 1:200, was the drug chosen because of its recognized bronchodilator activity. This agent was administered to 29 patients twice daily for 20 minutes over an eight-week period, with 0.5 ml. diluted with distilled water to a volume of 1 ml. and nebulized by a continuous flow of oxygen, about 4 liters per minute. Observations were made on the first day of the eight-week period, after the fourth week, and again after the eighth week. An attempt was also made to evaluate the patients' subjective impressions of bronchodilator therapy with and without added intermittent positive-pressure breathing.

Results

In table 1 are recorded the immediate results of treatment with power nebulization of the three bronchodilators, with intermittent positive-pressure breathing and without it. Improvement was noted after both procedures. Comparison of average results showed no significant difference in therapeutic effect. When the patients were considered individually, it appeared that 5 showed greater improvement after bronchodilator therapy given with intermittent positive pressure, 6 showed greater improvement after bronchodilator therapy alone, and the remaining 22 showed no difference in therapeutic effects. Thus, only 5 of the 33 patients appeared to be benefited specifically by the addition of intermittent positive-pressure breathing to bronchodilator therapy.

In tables 2 and 3 are recorded the results of short-term power nebulization therapy with the most effective bronchodilator for each patient. Table 2 shows the observations in 20 patients who received therapy without

intermittent positive-pressure breathing for two weeks, followed without interruption by therapy including it for two weeks. At the end of the first two-week period no significant change in pulmonary function was observed. After the second two-week period, during which intermittent positive-pressure breathing was used, there occurred a slight decrease in the average volume of deep respiration, while no change occurred in the average vital capacity or E–E′ percentage. Table 3 shows the observations in 13 other patients in whom the order of treatment was reversed, i. e., two weeks of treatment with intermittent positive-pressure breathing, followed without interruption by two weeks of treatment without it. At the end of the first two-week period an apparent slight decrease in pulmonary function was observed. After the second two-week period there was no further change.

Table 4 shows the results of continuous, extended treatment with oxygen-nebulized isoproterenol hydrochloride and added intermittent positive-pressure breathing. No significant improvement was noted after either four or eight weeks of treatment. Thus, at the end of 12 consecutive weeks of power-nebulized bronchodilator therapy, the 29 patients studied showed no fundamental improvement in pulmonary function. During the entire investigation, transitory responses to individual treatments occurred regularly. Their magnitude remained approximately constant throughout. Such temporary improvements presumably are helpful in retarding the progress of the disease, as well as providing considerable symptomatic relief.

Table 5 shows subjective estimates of the benefits of therapy. Of the 25 patients questioned, 11 preferred bronchodilator therapy that included intermittent positive-pressure breathing, 6 preferred therapy without it, and 8 had no preference. Eleven of the 25 patients expressed various complaints that they ascribed to intermittent positive-pressure breathing, notably pain or soreness in the chest, substernal distress, choking, and tachycardia. In some patients these symptoms were so severe that they requested that intermittent positive-pressure breathing be discontinued.

TABLE 1.—*Observations Made Before and After Therapy with Oxygen-Nebulized Bronchodilators, Comparison of Effects When Administered Without Intermittent Positive-Pressure Breathing and With Intermittent Positive-Pressure Breathing**

	Volume of Deep Respiration,† Liters				Inspiratory Vital Capacity, Liters				$\frac{E-E'}{VC} \times 100$, Expressed in %‡			
	Without IPPB§		With IPPB		Without IPPB		With IPPB		Without IPPB		With IPPB	
Patient	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	5.6	5.9	5.8	6.2	1.69	1.69	1.62	1.73	16.8	12.9	15.7	9.4
2	10.2	11.4	10.8	12.1	2.72	2.53	2.64	2.86	14.6	1.9	11.4	8.2
3	6.5	7.5	6.1	7.8	1.53	1.98	1.70	2.13	28.0	12.7	26.6	17.9
4	8.8	10.2	8.7	9.7	2.57	2.73	2.62	2.84	6.7	5.0	5.8	5.4
5	9.2	10.1	9.0	10.1	2.16	2.40	2.90	2.49	7.0	2.4	10.1	3.8
6	6.8	8.1	6.7	8.8	3.04	2.69	2.67	3.12	13.9	5.9	12.3	7.3
7	8.1	14.3	9.3	16.8	2.72	3.71	2.87	3.61	11.5	20.7	6.0	7.5
8	6.3	6.9	7.0	7.4	2.01	2.09	2.16	2.24	9.2	3.3	4.5	3.8
9	7.0	7.7	6.8	8.1	1.41	1.49	1.41	1.57	19.1	12.5	14.8	13.1
10	12.6	14.3	12.5	14.9	2.78	2.95	2.58	2.86	11.2	5.2	5.9	3.2
11	8.1	8.7	7.8	8.1	2.09	2.25	2.01	2.13	−1.4	0	−7.7	−4.1
12	9.5	10.7	8.8	8.7	2.44	2.53	2.39	2.42	14.2	8.5	12.4	9.6
13	6.3	7.3	6.3	7.0	1.34	1.51	1.44	1.46	8.3	5.1	14.3	4.0
14	7.6	8.8	7.5	10.2	1.96	2.09	2.01	2.13	12.0	10.8	9.3	2.6
15	12.8	13.2	12.8	14.2	2.75	2.79	2.73	2.93	9.3	7.4	10.4	8.6
16	14.0	14.9	14.0	15.5	2.69	2.94	2.86	3.12	6.2	−2.7	2.0	3.9
17	10.5	10.7	10.0	10.5	2.37	2.47	2.37	2.40	6.9	5.0	6.0	2.8
18	13.4	13.6	12.5	13.7	2.60	2.80	2.40	2.73	2.0	7.3	0.9	6.0
19	8.6	9.1	7.7	8.7	1.94	1.91	1.71	1.78	9.8	8.5	9.5	3.3
20	8.4	9.8	8.9	8.8	2.25	2.20	2.31	2.26	4.3	1.3	5.3	6.4
21	10.5	10.4	10.3	10.2	2.65	2.54	2.56	2.52	6.1	1.6	6.1	5.8
22	7.2	8.2	6.6	9.8	1.66	2.05	1.61	2.04	12.9	0.2	9.0	−2.2
23	9.0	9.5	9.1	8.8	1.79	1.81	1.77	1.75	12.2	5.9	8.0	7.6
24	7.0	8.8	7.0	8.1	1.61	1.88	1.76	1.80	5.4	3.7	13.7	6.1
25	9.1	10.5	9.1	10.6	2.06	2.21	2.09	2.28	12.7	5.1	13.6	6.0
26	8.4	9.0	10.4	10.2	1.73	1.75	1.80	1.80	5.7	11.7	8.1	9.9
27	12.5	12.9	12.3	12.5	2.78	2.70	2.67	2.75	5.8	1.9	7.7	8.5
28	9.9	10.2	9.2	9.7	2.53	2.73	2.32	2.46	2.1	0.8	4.3	1.6
29	14.6	14.9	13.4	13.9	3.20	3.08	2.94	3.04	13.4	5.1	10.6	5.6
30	8.9	10.0	8.1	10.6	2.32	2.62	2.22	2.91	13.8	1.9	7.6	2.2
31	7.5	8.8	7.8	8.8	1.93	1.85	1.88	1.98	9.7	8.2	15.9	8.8
32	11.6	11.8	11.6	11.2	2.37	2.37	2.43	2.45	8.7	5.7	6.1	6.0
33	8.0	8.3	8.6	9.7	1.60	1.71	1.91	2.01	−0.5	−1.2	8.3	5.9
Av	9.2	10.2	9.2	10.3	2.22	2.31	2.22	2.38	9.6	5.6	8.9	5.9

* Each figure represents an average of six separate tests. † Six consecutive maximal inspirations from position of quiet expiration.
‡ Intermittent positive-pressure breathing. § Represents "air-trapping." Decrease indicates improvement.

Comment

It is reasonably well established that therapy with intermittent positive-pressure breathing alone, without the simultaneous administration of a bronchodilator, does not benefit conditions associated with bronchospasm. Bronchodilators alone, on the other hand, without intermittent positive-pressure breathing, therapy, are

useful in such conditions. Our studies largely confirm the observations of Fowler, Helmholz, and Miller,[1d] who found that the addition of intermittent positive-pressure breathing did not enhance the value of bronchodilator therapy. No difference in average improvement after bronchodilator therapy could be demonstrated whether

TABLE 2.—*Averaged Observations in Twenty Patients Receiving Therapy with Oxygen-Nebulized Bronchodilators for Two Weeks Followed by Therapy with Oxygen-Nebulized Bronchodilators plus Intermittent Positive-Pressure Breathing for Two Weeks*

Time	Volume of Deep Respiration,* Liters		Inspiratory Vital Capacity, Liters		$\frac{E-E'}{VC} \times 100$, Expressed in % †	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Therapy with oxygen-bronchodilator						
1st day	9.9	10.5	2.36	2.40	7.2	4.3
End 2nd week	10.1	11.2	2.36	2.50	7.5	4.0
Therapy with oxygen-bronchodilator—IPPB ‡						
End 4th week	9.1	9.9	2.36	2.51	7.8	6.0

* Six consecutive maximal inspirations from position of quiet expiration.
† Represents "air-trapping." Decrease indicates improvement.
‡ Intermittent positive-pressure breathing.

or not intermittent positive-pressure breathing was used. This was true for both the immediate effect of treatment and for the observations after the two two-week periods of treatment, during one of which intermittent positive-pressure breathing was added to the bronchodilator therapy. Despite the lack of difference in the average results, there was some individual variation. Whereas in 27 of the 33 patients treatment without intermittent positive-pressure breathing was at least as effective as

TABLE 3.—*Averaged Observations in Thirteen Patients Receiving Oxygen-Nebulized Bronchodilators plus Intermittent Positive-Pressure Breathing for Two Weeks Followed by Oxygen-Nebulized Bronchodilators Without Intermittent Positive-Pressure Breathing for Two Weeks*

Time	Volume of Deep Respiration,* Liters		Inspiratory Vital Capacity, Liters		$\frac{E-E'}{VC} \times 100$, Expressed in % †	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Therapy with oxygen-bronchodilator-IPPB‡						
1st day	9.4	10.3	2.35	2.38	8.1	3.8
End 2nd week	8.3	9.8	2.19	2.41	11.1	4.3
Therapy with oxygen-bronchodilator						
End 4th week	8.9	9.3	2.14	2.23	9.0	4.6

* Six consecutive maximal inspirations from position of quiet expiration.
† Represents "air-trapping." Decrease indicates improvement.
‡ Intermittent positive-pressure breathing.

treatment with it, in 6 of the 33 treatment with it was superior. Of the 25 patients who gave subjective estimates of the comparative merits of the two methods of drug administration, 11 preferred the treatments with intermittent positive-pressure breathing, while 14 either had no preference or positively rejected intermittent positive-pressure breathing.

It is of some interest that there was rather poor correlation between the subjective and objective evaluations of intermittent positive-pressure breathing. This is understandable in view of the marked psychological effect of the imposing apparatus and procedure. The dramatic component of such therapy administered to impressionable patients may in part explain the discrepancy, which was observed in the patients who rejected the therapy as well as in those who preferred it.

The positive-pressure inflation of the pathological lungs found in the triad, consisting of pulmonary infection, fibrosis, and emphysema, is at least theoretically open to serious objection, unless incontrovertible evi-

TABLE 4.—*Averaged Observations in Twenty-Nine Patients Receiving Oxygen-Nebulized Isoproterenol (Isuprel) Hydrochloride plus Intermittent Positive-Pressure Breathing for Eight Weeks*

Time	Volume of Deep Respiration,* Liters		Inspiratory Vital Capacity, Liters		$\frac{E-E'}{VC} \times 100$, Expressed in % †	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
1st day	9.0	9.7	2.29	2.39	8.3	5.4
End of 4th week	9.1	9.8	2.29	2.35	8.7	3.5
End of 8th week	8.9	10.1	2.19	2.34	8.9	5.1

* Six consecutive maximal inspirations from position of quiet expiration.
† Represents "air-trapping." Decrease indicates improvement.

TABLE 5.—*Subjective Evaluation of Benefit Resulting from Therapy in Twenty-Five Patients*

Degree of Improvement	Type of Therapy		
	Oxygen-Nebulized Bronchodilator (Single Treatment)	Oxygen-Nebulized Bronchodilator-IPPB* (Single Treatment)	Oxygen-Nebulized Bronchodilator-IPPB (Eight-Wk. Course)
0	2	5	14
+	11	5	2
++	7	4	5
+++	5	10	3
++++	0	1	1

* Intermittent positive-pressure breathing.

dence for the value of such a procedure can be adduced. Since this evidence has not been consistently demonstrable, it is possible that intermittent positive-pressure breathing either alone or combined with bronchodilators is actually contraindicated. Further study is required for the resolution of this question.

In view of these considerations, it is reasonable to commence power nebulization of bronchodilators without added intermittent positive-pressure breathing. The simplicity of this therapy makes it easily adapted to self-administration in the home without any need for expensive apparatus. After the selection of an appropriate bronchodilator, a trial of power nebulization therapy should be made, preferably with some objective measurement of effect. An adequate volume of medicament should be delivered during treatments lasting approximately 15 minutes. Because of the marked variation in the therapeutic requirements of patients, schedules of therapy should be individually determined. If satisfactory improvement is not observed after an adequate

course of simple power nebulization bronchodilator therapy, the same treatment with added intermittent positive-pressure breathing may be given a trial.

Conclusions

Power nebulization of bronchodilators, which provides delivery of larger volumes of medicaments than is possible with hand nebulizers, is valuable in the management of bronchospastic states. The effect of the power nebulization of bronchodilator agents is not as a rule enhanced by the addition of intermittent positive-pressure breathing to the procedure. However, it must be noted that the lack of effectiveness of therapy with intermittent positive-pressure breathing in bronchospastic states does not controvert its well-established value in resuscitation, artificial respiration, and pulmonary edema.

Wilshire and Sawtelle boulevards (25) (Dr. Leslie).

1. (*a*) Motley, H. L.; Lang, L. P., and Gordon, B.: Use of Intermittent Positive Pressure Breathing Combined with Nebulization in Pulmonary Disease, Am. J. Med. **5**: 853-856 (Dec.) 1948. (*b*) Segal, M. S.; Salomon, A.; Dulfano, M. J., and Herschfus, J. A.: Intermittent Positive Pressure Breathing: Its Use in Inspiratory Phase of Respiration, New England J. Med. **250**: 225-232 (Feb. 11) 1954. (*c*) Smart, R. H.; Davenport, C. K., and Pearson, G. W.: Intermittent Positive Pressure Breathing in Emphysema of Chronic Lung Diseases, J. A. M. A. **150**: 1385-1390 (Dec. 6) 1952. (*d*) Fowler, W. S.; Helmholz, H. F., Jr., and Miller, R. D.: Treatment of Pulmonary Emphysema with Aerosolized Bronchodilator Drugs and Intermittent Positive Pressure Breathing, Proc. Staff Meet. Mayo Clin. **28**: 743-751 (Dec. 30) 1953. (*e*) Leslie, A.; Dantes, D. A., and Rosove, L.: Bronchodilator Activity of Three New Drugs in Patients with Pulmonary Emphysema, Dis. Chest **26**: 295-305 (Sept.) 1954.

2. Leslie, A.: Inspiratory-Expiratory Vital Capacity Test of Pulmonary Function, Am. J. Med. **13**: 809-812 (Dec.) 1952.

CLINICAL NOTES

NITROGEN MUSTARD IN TREATMENT OF ADVANCED CARCINOMA OF LUNG

ANALYSIS OF ONE HUNDRED NINETY-EIGHT CASES

Hurst B. Hatch, M.D.
Joseph K. Bradford, M.D.
and
Alton Ochsner, M.D., New Orleans

Evaluation of the results of the conventional methods of treatment of bronchogenic carcinoma by surgical excision and irradiation during the past 50 years has indicated the need for more effective therapy. During the last decade the possibility of discovering a preparation that might serve as an adjunct in the treatment of neoplastic disease has been viewed with increasing interest. Consequently, an intensive search has been made for a chemical that would have a selective, yet lethal, effect on the neoplastic cell. As a result of this search, a group of cytotoxic chemical agents has been discovered that has proved promising. One of these, nitrogen mustard (methyl-bis [β-chloroethyl] amine), was first utilized in the treatment of neoplastic disease by Gilman and coworkers [1] in 1943. Since then, frequent reports concerning its use in patients with advanced bronchogenic carcinoma have appeared in the literature. Our experience with this chemical in 198 patients with advanced carcinoma of the lung during the six-year period ending July 31, 1953, forms the basis of this report. A preliminary report of the results in the first 68 cases in this series was made in 1951.[2]

From the Section on Chest Diseases (Drs. Hatch and Bradford) and the Department of Surgery (Dr. Ochsner), Ochsner Clinic.

Material

One hundred sixty-nine of the patients were men and 29 were women, or a ratio of 5.8 to 1. The distribution of patients according to age groups is shown in table 1. One hundred fifty patients received one course of nitrogen mustard, and the remainder received two or more courses at intervals of from eight weeks to one year. A course consisted of a daily dose of nitrogen mustard calculated on the basis of 0.1 mg. per kilogram of body weight for four days. Twenty-five patients also were given roentgen therapy, five receiving it prior to the nitrogen mustard and the remainder after at least one course of the drug. In addition, four were given pteroyl-triglutamic acid (Teropterin) and one, diethylstilbestrol.

TABLE 1.—*Age and Sex Distribution of 198 Patients with Advanced Bronchogenic Carcinoma Treated with Nitrogen Mustard*

Age, Yr.	Male	Female
30-34	4	0
35-39	3	2
40-44	14	2
45-49	25	4
50-54	28	5
55-59	34	7
60-64	32	4
65-69	17	3
70-74	10	1
75-79	1	1
80 and over	1	0
Total	169	29

Toxic Reactions

Toxic reactions from nitrogen mustard have been classified as immediate and delayed. The immediate reactions include thrombophlebitis at the site of injection, nausea and vomiting, anorexia, malaise, headache, vertigo, and diarrhea. The delayed reactions, such as anemia, granulocytopenia, lymphocytopenia, thrombocytopenia, and reticulocytopenia, are not common but obviously can be serious. It should be pointed out that these toxic reactions are a direct result of the drug and are not in any way related to the alarm reaction of Selye. The effect of the tertiary amines in patients with hepatic or renal disease has been found to be of no serious nature. Almost one-half of the patients in the present series (47.4%) had no untoward effects from the nitrogen mustard. The reactions experienced by the remainder (104 patients) are similar to those reported by other observers. Of the immediate reactions, 97 patients had nausea and/or vomiting; 2 had rash; and one, diarrhea. Of the delayed reactions, one patient had jaundice; 18, anemia; 7, leukopenia; and one, granulocytopenia. As reported previously, no prognostic significance could be attributed to the presence or absence of these reactions. During the latter three years of this study, the incidence of the delayed and more serious complications has been practically nil, but we can offer no explanation for this.

Results

Reported results have varied from beneficial effects, in 40 to 70% of cases, to little, if any, relief.[3] All authors, however, agree that improvement is usually limited to relief of cough, dyspnea, malaise, anorexia, and even hemoptysis and to increase in strength and weight; but they feel that life is not prolonged significantly. There have also been reports of reduction in the size of the tumor, in the volume of pleural effusion, and even in the extent of involvement of metastatic sites. Improvement is evident within two or three weeks and lasts for approximately three to four months.

TABLE 2.—*Symptomatic Response to Nitrogen Mustard According to Histological Type in 198 Patients with Advanced Bronchogenic Carcinoma*

Type	Response				Total
	0	++	+++	++++	
Epidermoid carcinoma	27	10	16	3	56
Undifferentiated	43	13	5	6	67
Adenocarcinoma	15	6	4	4	29
Oat-cell carcinoma	1	1	1	4	7
Undetermined	21	6	8	4	39
Total	107	36	34	21	198

The responses to therapy in this series of cases were classified in three categories. The response was considered as 2+ if the patient experienced a general sense of well-being but showed no evidence of specific effect. A 3+ response was one in which there was definite diminution or disappearance of two or more of such symptoms as cough, dyspnea, weakness, malaise, amount of sputum, hemoptysis, and anorexia. It was classified as 4+ if, in addition, the patient gained weight and was able to maintain some working capacity and/or some improvement could be demonstrated radiologically. The results were correlated with the histological type.

Ninety-one patients (45.9%) obtained symptomatic relief of varying degree, and 107 (54.1%) showed no response at all (table 2). Of the 198 patients, only 22 are living. The survival rate according to histological types is shown in table 3.

Of the 150 patients who received only one course of nitrogen mustard, 43 (28.7%) showed some response, whereas, of the 48 who received more than one course, a symptomatic response of some degree was noted in 45 (93.7%). This would suggest that, even if no response is obtained after one course, it is worthwhile to repeat the course. As far as we have been able to determine, this observation is contrary to that of any previous reports.

TABLE 3.—*Longevity According to Histological Type in 198 Patients with Advanced Bronchogenic Carcinoma Treated with Nitrogen Mustard*

Type	Survival, Mo.	
	Shortest	Longest
Adenocarcinoma	¼	14
Epidermoid carcinoma	1	35
Oat-cell carcinoma	¾	25
Undetermined	1	36
Undifferentiated	1	32

Although the number of patients in this series receiving both roentgen therapy and nitrogen mustard is too small to use as a basis for definite conclusions, such a combination appears to be the most efficacious method of treatment of advanced carcinoma of the lung. The best results in the present series were obtained when roentgen therapy followed the original course of nitrogen mustard. There appeared to be no difference in the response of the patients in this series whether or not the lung had been resected. There also was no difference in the responses of the different histological types of tumors to nitrogen mustard therapy.

Conclusions

The results of a study in 198 patients substantiate those of previous observers that between 40 and 50% of patients with advanced bronchogenic carcinoma obtain symptomatic relief from nitrogen mustard (methyl-bis [β-chloroethyl] amine) therapy. Contrary to most reports, this study suggests that it is efficacious to repeat the course of nitrogen mustard at regular eight-week intervals of time, regardless of the response to the first course. It appears that the combination of multiple courses of nitrogen mustard and deep roentgen-ray therapy will materially improve the therapeutic status of advanced bronchogenic carcinoma.

Nitrogen mustard represents a most valuable adjunct to the palliative therapy of advanced bronchogenic carcinoma, but it must be realized that this chemical is not carcinolytic and that its beneficial effects are only transient.

3503 Prytania St. (15) (Dr. Hatch).

1. Gilman, A.; Goodman, L. S.; Philips, T. S., and Dougherty, T.: Unpublished data.

2. Ayers, W. B.: Nitrogen Mustard in the Treatment of Advanced Carcinoma of the Lung: Analysis of 68 Cases, New Orleans M. & S. J. **103**: 290-294 (Jan.) 1951.

3. Rhoads, C. P.: Report on Cooperative Study of Nitrogen Mustard (CHN_2) Therapy of Neoplastic Disease, Tr. A. Am. Physicians **60**: 110-117, 1947. Craver, L. F.: Nitrogen Mustards: Clinical Use, Radiology **50**: 486-493 (April) 1948. Skinner, E. F.; Carr, D., and Denman, W. E.: The Treatment of Inoperable Bronchiogenic Carcinoma with Methyl-Bis, J. Thoracic Surg. **17**: 428-438 (Aug.) 1948. Lynch, J. P.; Ware, P. F., and Gaensler, E. A.: Nitrogen Mustard in the Treatment of Inoperable Bronchiogenic Carcinoma, Surgery **27**: 368-385 (March) 1950.

SERUM GLUTAMIC OXALACETIC AMINOPHERASE (TRANSAMINASE) IN HEPATITIS

Felix Wróblewski, M.D.
and
John S. LaDue, M.D., Ph.D., New York

Glutamic oxalacetic aminopherase (transaminase) is widely distributed in animal tissues. Its greatest activity has been found in homogenates of heart muscle, skeletal muscle, brain, liver, and kidney, in decreasing order. This enzyme activity has been found in all animal and human serums tested, and the activities are comparable whether the analysis is done chromatographically or spectrophotometrically.[1] It has been demonstrated that serum glutamic oxalacetic aminopherase activity increases 2 to 20 times normal after acute myocardial infarction and may rise 20 to 100 times normal in hepatitis due to toxic or infectious agents.[2] The present study is an

From the Sloan-Kettering Institute and the Medical Service of the Memorial Center for Cancer and Allied Diseases.

extension of a preliminary report on serum glutamic oxalacetic aminopherase alterations in liver disease, with particular emphasis on hepatitis. The study to be reported will describe the activity in hepatitis and discuss the usefulness of determination of the activity in the diagnosis and management of hepatitis and in the epidemiological course of infectious hepatitis.

Serum glutamic oxalacetic aminopherase levels are not elevated in patients with infectious, neoplastic, degenerative, reactive, allergic, or congenital disease states unless evidence of acute damage to the liver, heart, or skeletal muscle is present. We have previously postulated that the probable mechanism for increase in activity is effected by release of the enzyme from damaged cells into the blood stream.[3]

Methods and Material

Serum glutamic oxalacetic aminopherase levels are measured by the spectrophotometric method previously described.[4] The mean activity of adult human serum is 22.1 units, with a standard deviation of 6.8. The normal range of activity for adult human serums is 5 to 40 units determined at a temperature of 20 C. Patients with infectious hepatitis, homologous serum hepatitis, and toxic hepatitis were carefully followed in the hospital over a 3-week to 12-month period. Serum glutamic oxalacetic aminopherase activity was determined at frequent intervals, and the following liver function tests were also obtained: bilirubin, urinary urobilinogen, alkaline phosphatase, cephalin flocculation, thymol turbidity, albumin-globulin ratio, and in some cases sulfobromophthalein (Bromsulphalein) excretion. Similar studies done upon patients with cirrhosis, metastatic liver disease, and extrahepatic obstructive jaundice of varying etiology will be outlined as they relate to the differential diagnosis. At Letchworth Village, Thiells, N. Y., an institution for the mentally defective, 151 patients living in a communal building were exposed to three of their inmates who developed infectious hepatitis. The entire population of this cottage had analyses of serum glutamic oxalacetic aminopherase activity once or twice weekly over a three-month period of study, together with some of the liver function tests mentioned above. (Dr. George Jervis, director of laboratories at Letchworth Village, is collaborating in the epidemiological study of infectious hepatitis. This study will subsequently be reported in detail.)

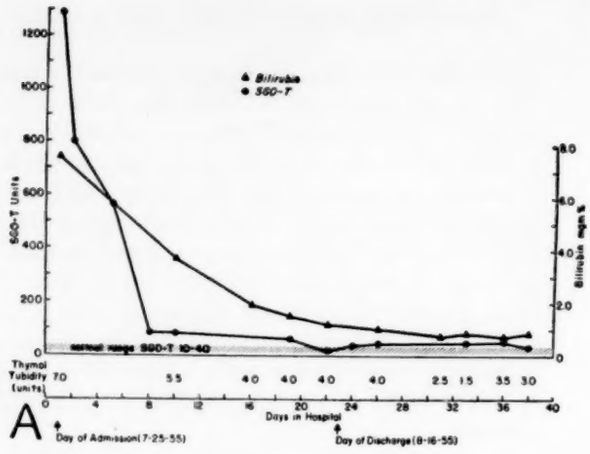
Results

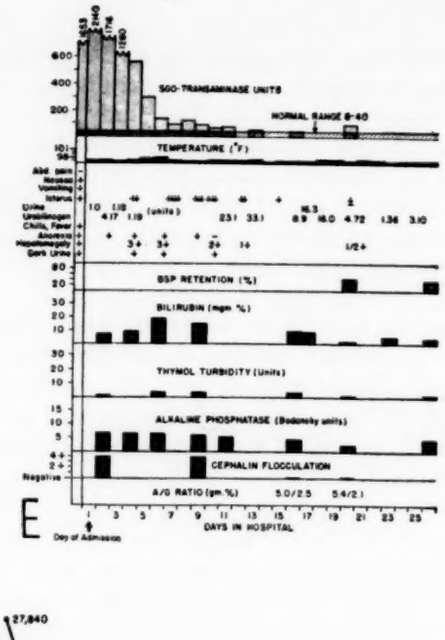
Endemic Infectious Hepatitis.—Twenty patients with infectious hepatitis, 15 of whom were studied in Letchworth Village, provided an opportunity to observe this disease in a closed, institutional environment. Seventeen were ill one to two weeks prior to hospitalization, and three had symptoms for three to five weeks prior to hospitalization. The patients complained of anorexia, nausea, vomiting, pruritus and generalized malaise. All of the patients were jaundiced, 17 had moderate enlargement of the liver, and in 4 the spleen was palpable. The serum glutamic oxalacetic aminopherase activity was more than 1,000 units on admission in four patients and ranged from 800 to 1,000 in another four individuals; in six patients an activity of 500 to 800 units was present and in five, 300 to 500 units; in one patient the determination was not done until the 23rd day of his illness, when the level was 60 units. The figure, *A*, describes the alterations in serum glutamic oxalacetic aminopherase in a patient characteristic of this group. The activity returned to normal levels within four weeks in 16 patients and in the fifth, sixth, seventh, and eighth week in four instances. Two or more of the tests of liver function were grossly abnormal on admission and in some instances remained abnormal although the serum glutamic oxalacetic aminopherase activity had fallen to 40 units or below in 17 of the 20 patients. All the patients recovered.

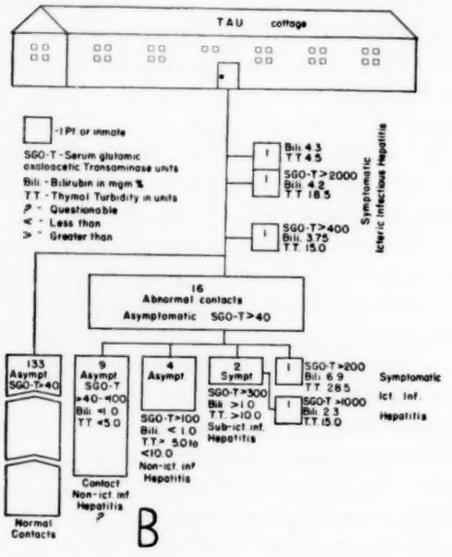
In one cottage housing 154 inmates, 3 developed infectious hepatitis, for which they were immediately hospitalized. At the same time that the three patients with infectious hepatitis were hospitalized, serums were drawn once weekly from the remaining 151 occupants. Sixteen inmates had elevation of activity above 40 units during the first week of the study. The remaining 133 had persistently normal activity during the remaining three months of observation (figure, *B*). The 16 patients with increased activity were divided into three groups. Nine (group 1) had activity above 40 but less than 100 units; all had normal liver function tests, and in all the serum glutamic oxalacetic aminopherase activity fell to normal in less than 28 days. The second group of four (group 2) had activity varying from 100 units to 350 units; the serum bilirubin level in all was less than 1 mg. per 100 cc., but the thymol turbidity reaction was above 5 but less than 10 units. The remaining three inmates (group 3), two of whom were hospitalized, had peak serum glutamic oxalacetic aminopherase levels ranging from 390 to 1,800 units; the serum bilirubin level was 2.3, 4.5, and 6.9 mg. per 100 cc., the thymol turbidity 18.0, 20.0, and 26.5 units respectively. None of the individuals with normal serum glutamic oxalacetic aminopherase activity developed any symptoms or signs of hepatitis over the three-month period of study. One individual followed over a 73-day period was successfully seen to pass from group 1 to group 3, first having an aminopherase activity of 76 units, which rose to 168 in 30 days and on the 73rd day was 1,008, when the serum bilirubin level was 2.3 mg. per 100 cc. and the thymol turbidity 15.0 units.

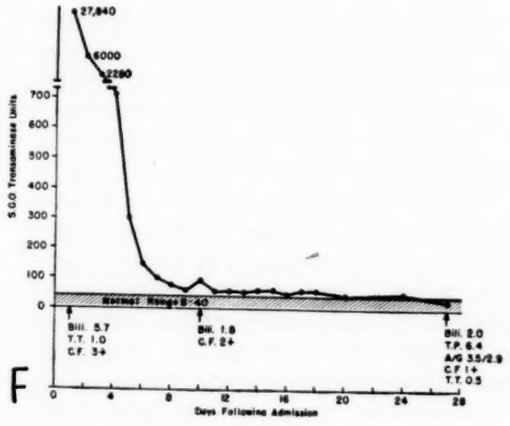
Five patients with infectious mononucleosis exhibited elevations in activity of from 80 to 300 units over a three-week period. None developed clinical jaundice, but all had slight elevations of bilirubin level and abnormal sulfobromophthalein retention, thymol turbidity, and cephalin flocculation reactions. Other patients with infectious mononucleosis uncomplicated by "hepatitis" have all had normal activity.

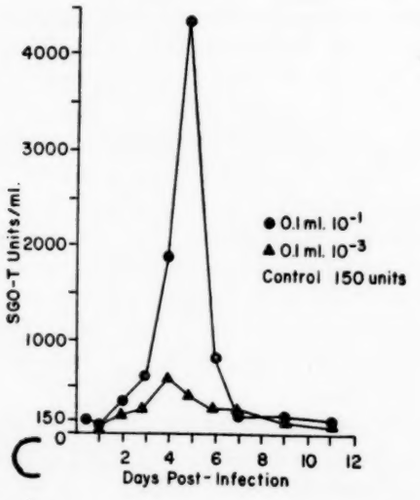
Aminopherase activity was followed in experimentally induced mouse-virus hepatitis. The figure, *C*, shows the changes in activity in these animals following a large and a small viral inoculant. It was also shown in mouse-virus hepatitis that the increase in enzyme activity is roughly proportional to the degree of liver cell damage, to the amount of the virus inoculant, and to the titer of the virus in the serum and liver tissue (figure, *D*).

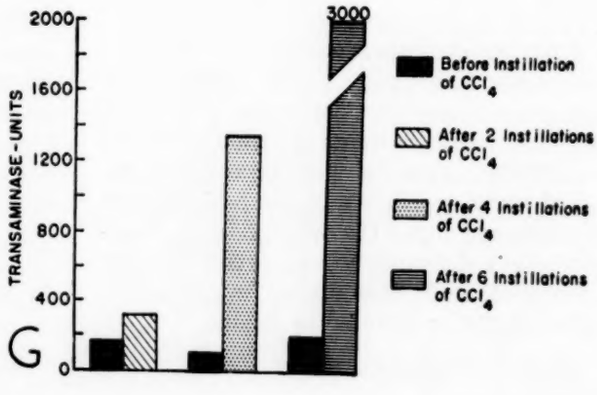

Bilirubin
SGO-T
SGO-T Units
Bilirubin mgm %
Thymol Turbidity Units
Days in Hospital
Day of Admission (7-25-55)
Day of Discharge (8-16-55)
A

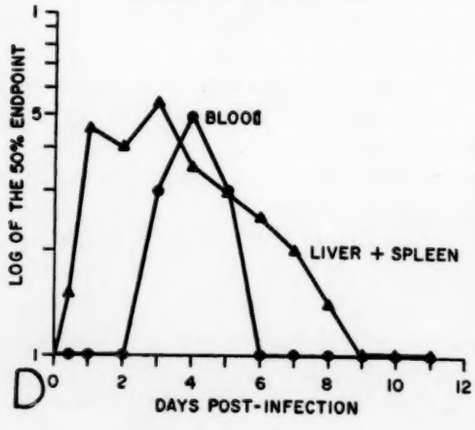

SGO-TRANSAMINASE UNITS
NORMAL RANGE 8-40
TEMPERATURE (°F)
BSP RETENTION (%)
BILIRUBIN (mgm %)
THYMOL TURBIDITY (Units)
ALKALINE PHOSPHATASE (Bodansky units)
CEPHALIN FLOCCULATION
A/G RATIO (gm %)
DAYS IN HOSPITAL
Day of Admission
E

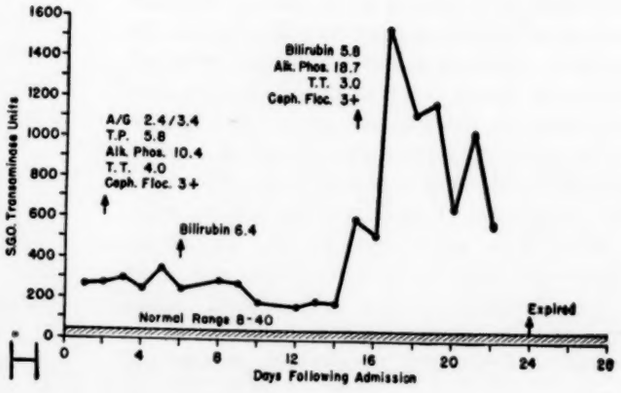

TAU cottage
= 1 Pt or inmate
SGO-T - Serum glutamic oxaloacetic Transaminase units
Bili. - Bilirubin in mgm %
T.T. - Thymol Turbidity in units
? - Questionable
< - Less than
> - Greater than
Bili 4.3
T.T 4.5
SGO-T > 2000
Bili. 4.2
T.T 18.5
SGO-T > 400
Bili. 3.75
T.T. 15.0
Symptomatic Icteric infectious Hepatitis
16
Abnormal contacts
Asymptomatic SGO-T > 40
133
Asympt
SGO-T < 40
Normal Contacts
9
Asympt
SGO-T
>40-<400
Bili. <1.0
T.T. <5.0
Contact
Non-ict. inf
Hepatitis
4
Asympt
SGO-T > 100
Bili. < 1.0
T.T. > 5.0 to < 10.0
Non-ict. inf
Hepatitis
2
Sympt
SGO-T > 300
Bili. > 1.0
T.T. > 10.0
Sub-ict. inf.
Hepatitis
1
SGO-T > 200
Bili. 6.9
T.T. 28.5
1
SGO-T > 1000
Bili. 2.3
T.T. 15.0
Symptomatic
Ict. Inf.
Hepatitis
B


27,840
6000
2280
S.G.O. Transaminase Units
Normal Range 8-40
Bili. 5.7
T.T. 1.0
C.F. 3+
Bili. 1.8
C.F. 2+
Bili. 2.0
T.P. 6.4
A/G 3.5/2.9
C.F. 1+
T.T. 0.5
Days Following Admission
F


SGO-T Units/ml.
● 0.1 ml. 10⁻¹
▲ 0.1 ml. 10⁻³
Control 150 units
Days Post-Infection
C


TRANSAMINASE-UNITS
Before Instillation of CCl4
After 2 Instillations of CCl4
After 4 Instillations of CCl4
After 6 Instillations of CCl4
G


LOG OF THE 50% ENDPOINT
BLOOD
LIVER + SPLEEN
DAYS POST-INFECTION
D


S.G.O. Transaminase Units
A/G 2.4/3.4
T.P. 5.8
Alk. Phos. 10.4
T.T. 4.0
Ceph. Floc. 3+
Bilirubin 6.4
Bilirubin 5.8
Alk. Phos. 18.7
T.T. 3.0
Ceph. Floc. 3+
Normal Range 8-40
Expired
Days Following Admission
H

It appears likely that the increase of aminopherase activity in the serum probably results from the release of intracellular enzyme into the blood stream from the damaged liver cells.[5]

Homologous Serum Hepatitis.—Twelve patients had homologous serum hepatitis, which was apparently transmitted in six by various injections and in six by transfusions. Anorexia, nausea, emeses, pruritus, dark urine, and, in some instances, light-colored stools were the symptoms proferred by the patients. All had hepatomegaly and jaundice of varying degree, and in three the spleen was palpable. Hospital admission was within 10 days of the onset of the illness in four patients and after 15 to 30 symptom-days in the remainder. The aminopherase activity in this group of patients varied from 500 to 2,500 units during the first week of the illness.

Three patients had levels of 2,000 or more units and six of 750 to 1,500 units; in the remaining three patients the level, taken after 10 or more days of illness, was 220, 176, and 76 units. In five of the patients with homologous serum hepatitis the usual liver function tests remained abnormal 10 days to three months longer than it took for the aminopherase to return to normal limits. Two patients died. In one, the aminopherase activity remained at 250 units during the five months of her illness. The second died on the 150th day of her illness of hepatic failure complicated by cardiac decompensation; the aminopherase level fell from 1,245 to 50 units on the 38th hospital day, only to rise to 921 units eight days before death. The figure, *E*, depicts the course of illness in a 32-year-old man who was admitted to the hospital complaining of generalized malaise of one week's duration. On the second hospital day, aminophpherase activity was 2,140 units, which fell gradually within 20 days to normal. All the liver function tests performed were abnormal on the day of admission. The sulfobromophthalein retention and thymol turbidity reaction were still abnormal for 40 or more days, and the bilirubin level was 3 mg. per 100 cc. two months after admission. The secondary rise in aminopherase level to 98 units was associated with the patient's resumption of activity, and the return of the level to normal followed two additional weeks of bed rest.

Toxic Hepatitis.—Marked aminopherase elevations were seen in two patients who were accidentally exposed to carbon tetrachloride fumes two days prior to hospitalization. Both complained of nausea, vomiting, headache, and generalized malaise, were moderately icteric, and had minimal hepatomegaly (figure, *F*). The elevation in aminopherase level of 27,800 and 12,300 units respectively 48 hours after exposure is striking, with a rapid return toward normal within seven days. Toxic hepatitis was produced in rats by the administration of carbon tetrachloride, and the elevation in aminopherase level was found to be proportional to the extent of liver cell damage and to the amount of the toxin administered (figure, *G*).[6] The aminopherase activity was followed in a patient receiving pyrazinamide treatment for tuberculosis. This patient developed elevation of activity three weeks before he developed clinical or other laboratory evidence of toxic hepatitis. When the drug was withdrawn, the aminopherase activity returned to normal.

A, alterations in serum glutamic oxalacetic aminopherase (SGO-T) level in a patient with infectious hepatitis. Note the lack of correlation between the changes in liver function tests and aminopherase activity. *B*, categorization of aminopherase activity in 151 inmates exposed to three patients with infectious hepatitis. *C*, aminopherase activity in mice after intraperitoneal inoculation of 0.1 ml. of 10^{-1} and 0.1 ml. of 10^{-2} dilution of hepatitis virus. *D*, amount of virus in blood and viscera after intraperitoneal inoculation of 0.1 ml. of 10^{-1} dilution of hepatitis virus into mice. *E*, clinical and laboratory data of a patient with homologous serum hepatitis. *F*, aminopherase activity alterations in a patient exposed to carbon tetrachloride 48 hours prior to hospital admission. *G*, comparison of peak aminopherase (transaminase) activity in rats before and after varying amounts of intragastrically administered carbon tetrachloride. *H*, aminopherase activity in a patient with Laennec's cirrhosis complicated by hepatitis.

Comment

Measurement of the serum glutamic oxalacetic aminopherase activity during the acute phase of hepatitis, whatever its cause, usually permits differentiation of jaundice due to this cause from that due to cirrhosis, extrahepatic obstruction of the biliary ducts, liver metastases, and hemolysis. Of 28 patients with cirrhosis of the liver, 8 had normal aminopherase activity; in 14 it varied from 41 to 100 units, and in 6 the level was above 100 units but less than 300, unless complicating hepatitis was also present. The figure, *H*, shows the activity in a patient with Laennec's cirrhosis. The aminopherase level during the first 15 days varied from 180 to 300 units in association with grossly abnormal liver function tests. On or about the 16th day, the level rose to 1,600 units, falling to 600 units the day before death. At autopsy, Laennec's cirrhosis was apparent on gross examination, but microscopic study revealed the presence of complicating hepatitis.

Extrahepatic biliary obstructive jaundice is characterized by increments in aminopherase activity of approximately 200 units. The enzyme level rapidly falls to normal after relief of the biliary obstruction. The activity usually falls to normal within two to eight days, while the alkaline phosphatase level is elevated for several days longer in all the patients we have followed. Although our experience in this group of patients is somewhat limited, there has been no exception in 10 patients studied and in one experimental animal.

Twenty of 22 patients with proved liver metastases had increased aminopherase activity on one or more determinations. The usual liver function tests were run concomitantly, and it is of interest that the only laboratory evidence of liver involvement was elevation of the aminopherase level in seven patients. In 13 the level ranged from 60 to 230 units, but the alkaline phosphatase level and at times other liver function tests were also abnormal. In two instances the metastases were judged to be very small and the aminopherase activity as well as all other liver function tests done were normal. It is pertinent that every one of 50 patients who had moderate to marked elevation of the alkaline phosphatase level secondary to bone metastases in the absence of hepatic metastases had normal aminopherase activity.[7]

Surgical trauma to skeletal muscle, acute myocardial infarction, active rheumatic carditis, and any process associated with acute injury to skeletal muscle or heart

muscle may result in increased aminopherase activity. These clinical situations present little or no confusion diagnostically inasmuch as they appear in different clinical settings and are reflected by alterations in aminopherase of significantly different magnitudes and serial changes.

Both experimental and clinical hepatitis are associated with rises in aminopherase activity. In experimental viral hepatitis the rise in activity is proportional to the size of the viral inoculum; in the clinical setting, the peak rise in activity appears to be related to the severity of the disease. Relapses during the clinical course of hepatitis are reflected by superimposed rises in aminopherase activity at a time when the enzyme activity is expected to return toward or to the normal range. Evidence at hand indicates that, one to four weeks prior to the appearance of jaundice, patients with hepatitis may manifest significant increments in aminopherase activity. This permits early diagnosis of either homologous serum hepatitis or infectious hepatitis in the preicteric or prodromal phase. Further study is required to ascertain whether minor aminopherase elevations in the absence of other laboratory evidence of hepatitis accurately reflect the occurrence of nonicteric viral hepatitis.

The aminopherase activity in hepatitis appears to correlate well with the clinical status. Peak levels of aminopherase are found usually when the patient is sickest, as manifested by lethargy, fever, anorexia, nausea, and vomiting. Conversely, the patients become more alert and afebrile and have return of appetite shortly after the usually precipitous fall of aminopherase occurs. At a time when the aminopherase level is falling, the bilirubin level may remain elevated, continue to rise, or fall slightly. The other tests of liver function usually are abnormal for days or weeks after the aminopherase activity has returned to normal. The therapeutic implications, as well as recent observations, suggest that it is quite safe to begin ambulation at a time when the tests of liver function are still abnormal. Occasionally, secondary rises or peaks of aminopherase activity occur within a few days after premature ambulation and return toward normal after the resumption of bed rest. Further experience is needed to evaluate the use of aminopherase activity as an index for ambulation of patients with hepatitis.

Conclusions

Preliminary epidemiological data have shown that the serum glutamic oxalacetic aminopherase (transaminase) activity rises one to four weeks before other clinical or laboratory evidence of liver injury becomes manifest. This then permits diagnosis of hepatitis in the preicteric stage and suggests that epidemics in a closed environment may be controlled by isolation of contacts who demonstrate increased aminopherase activity. The possible applications of these observations to control of infectious and homologous serum hepatitis are presently under study. The fact that increased aminopherase activity has been found to precede the development of jaundice resulting from chlorpromazine and pyrazinamide suggests that aminopherase activity may be used as a tool to anticipate and thereby prevent toxic hepatitis in patients who are receiving potentially hepatotoxic drugs.

444 E. 68th St. (21) (Dr. Wróblewski).

1. LaDue, J. S.; Wróblewski, F., and Karmen, A.: Serum Glutamic Oxalacetic Transaminase in Human Acute Transmural Myocardial Infarction, Science **120**: 497-499, 1954.
2. Wróblewski, F., and LaDue, J. S.: Serum Glutamic Oxalacetic Transaminase Activity as an Index of Liver Cell Injury: A Preliminary Report, Ann. Int. Med. **43**: 345-360, 1955. Footnote 1.
3. Nydick, I.; Wróblewski, F., and LaDue, J. S.: Evidence for Increased Serum Glutamic Oxalacetic Transaminase (SGO-T) Activity Following Graded Myocardial Infarcts in Dogs, Circulation **12**: 161-168, 1955.
4. Karmen, A.; Wróblewski, F., and LaDue, J. S.: Transaminase Activity in Human Blood, J. Clin. Invest. **34**: 126-133, 1955.
5. Friend, C.; Wróblewski, F., and LaDue, J. S.: Glutamic Oxalacetic Transaminase Activity of Serum in Mice with Viral Hepatitis, J. Exper. Med. **102**: 699-704, 1955.
6. Molander, D. W.; Wróblewski, F., and LaDue, J. S.: Serum Glutamic Oxalacetic Transaminase as an Index of Hepatocellular Integrity, J. Lab. & Clin. Med. **46**: 831-839, 1955.
7. Wróblewski, F., and LaDue, J. S.: Serum Glutamic Oxalacetic Transaminase as an Index of Liver Cell Injury Due to Cancer, Cancer, **8**: 1155-1163, 1955.

THE L. E. CELL AS A MANIFESTATION OF DELAYED HYDRALAZINE INTOXICATION

Phillip Comens, M.D.
and
Henry A. Schroeder, M.D., St. Louis

A syndrome simulating collagen disease has been reported [1] in some patients receiving hydralazine (Apresoline) hydrochloride for at least six months in order to control arterial hypertension. The typical L. E. cell has sometimes been found in the peripheral blood of such individuals, especially when administration of the drug was continued after the appearance of arthralgia or arthritis.[1d] Symptoms at first resembled rheumatoid arthritis of various degrees of severity; in more advanced forms manifestations of disseminated lupus erythematosus appeared. This report represents the first of a series designed to study the action of hydralazine in relation to collagen disease. A second will be concerned with the production of a similar syndrome in dogs.

Method

Two hundred thirty-six L. E. preparations were made on blood from 105 hypertensive patients receiving hydralazine. Ninety-seven patients had no symptoms of arthritis, and eight had arthritis plus the physical and laboratory abnormalities that are associated with collagen disease.[1d] Of over 400 patients receiving hydralazine continuously, collagen disease with or without positive smears has appeared in approximately 8%. The incidence of this disorder in our series has not increased since our first full report [1d] in spite of larger numbers. Smears positive for L. E. cells have been found in only 11, 8 of whom were selected for this study. The patients came from all socioeconomic strata; approximately half were men; both Negro and white individuals were included. With the use of the two hour clot technique of Zimmer and Hargraves,[2] a pair of slides was made from

From the Hypertension Division, Department of Internal Medicine, Washington University School of Medicine, and Barnes Hospital.
This study was supported by a grant-in-aid from the National Heart Institute, United States Public Health Service, and the Lasdon Foundation.

each sample of blood. Each slide was examined for at least 20 minutes on two occasions. A preparation was considered positive (group 1) when many typical L. E. cells with homogenous hyalinized inclusion bodies were seen. A preparation was considered suspicious (group 2) when an occasional or rare L. E. cell was found, according to the criteria of Hargraves.[3] All other preparations were considered negative (group 3). Nucleophagocytosis and nuclear fragmentation were noted. When possible a cephalin-cholesterol flocculation test was obtained simultaneously with the L. E. preparation.

Results

The results are shown in the table. In seven of the eight patients with positive L. E. cell preparations (group 1), the cephalin-cholesterol flocculation of blood was abnormal prior to the appearance of the L. E. and 9 in group 3. In five cases, after the onset of the clinical picture of this disorder the cephalin-cholesterol flocculation value was elevated while the L. E. preparation was negative, later becoming positive. In two cases, both tests were negative before and at the onset of the syndrome, but serial tests later revealed a 3 or 4+ cephalin-cholesterol flocculation approximately one week before L. E. cells finally appeared. In a third case the L. E. test remained positive three months after discontinuation of hydralazine therapy, even though the cephalin-cholesterol flocculation had returned to normal and all symptoms had disappeared.

Comment

There is little difficulty in the recognition of the typical L. E. cell with its hyalinized inclusion body and hematoxylin-staining bodies. Recently, however, controversy

L. E. Studies on 105 Hypertensive Patients Treated with Hydralazine

Cases	Race	Sex	Age, Yr.	Known Duration of Hypertension, Yr.	Duration of Hydralazine Therapy, Mo.	Total Dose Hydralazine, Gm.	3+ and 4+ Cephalin Flocculation	Nucleophagocytosis	Fragmented Pyknotic Nuclei
Group 1, Positive L. E.—7.6%									
8	25% N 75% W	62% F 38% M	32-70 ..	1-13	6-30 ..	90-637	100%	25% (50% M) (50% F)	38% (100% F)
Mean	...	..	49	5.1	20	307.4 (175.8 F) (434.3 M)			
Group 2, Suspected Cases of L. E. (9.6%) *									
1	W	M	36	13.0	22	262.25	Neg.	..	..
2	W	F	41	3.5	31	227.03	Neg.	..	+
3	W	F	51	6.0	3	45.00	Neg.	..	..
4	W	F	63	0.6	6	72.00	Neg.	..	+
5	W	M	52	24.0	32	486.75	Neg.	+	..
6	W	F	63	2.9	33	133.37	Neg.	..	+
7	W	M	53	10.0	10	59.28	Neg.	..	..
8	N	F	48	10.0	34	477.90	Neg.	+	..
9	N	F	45	5.0	3	16.80	Neg.	..	..
10	W	M	49	5.0	6	36.00	Neg.	..	..
Range	20% N 80% W	60% F 40% M	36-63 ..	0.6-24	4-34 ..	16-486.75	0%	20% (50% M) (50% F)	30% (100% F)
Mean	...	..	50.1	8.0	18.0	194.6 (161.8 F) (243.8 M)			
Group 3, Negative L. E. (82.8%)									
87	26.4% N 73.6% W	52% F 48% M	6-71 ..	0.1-48	1.0-48 ..	2.6-761.4	5.7%	6.9% (33% M) (66% F)	10.3% (33% M) (66% F)
Mean	...	..	49.2	7.2	17.5	218.8 (201 F) (238 M)			

* Blood preparations contained 1 to 3 typical cells per slide in each of 2 to 6 slides.

cell. Of the 97 asymptomatic patients, 10 had smears showing occasional or rare L. E. cells (group 2); in none of the 10 was the cephalin-cholesterol flocculation test 3 or 4+. Five of the remaining 87 asymptomatic patients with normal blood smears (group 3) simultaneously exhibited 3 or 4+ cephalin-cholesterol flocculations.

Nucleophagocytosis was found in all smears from 10 individuals; it was present in 2 of the 8 of group 1 and 2 of the 10 suspicious cases of group 2. Nucleophagocytosis was considered to be present when there were considerable numbers of cells with lysing chromatin networks but not with intact chromatin nuclear patterns. Fragmented and pyknotic nuclei were present in 15, of which 12 were from women; 3 in group 1, 3 in group 2, and speculation have arisen as to the specificity of these cells in collagen disease. Perhaps some of the confusion is due to the close resemblance of nucleophagocytic cells to borderline L. E. cells. In this study we have restricted ourselves to the most rigid criteria,[3] recognizing, however, that nucleophagocytosis may be a precursor of the L. E. phenomenon.

There appeared little or no significant differences in the presence of the disorder in the three groups as to race, age, and sex. In general, those with positive smears were the more severely hypertensive, as exemplified by the large doses of hydralazine required for adequate control of blood pressure. Of the five asymptomatic patients with cephalin-cholesterol flocculations of 3 or 4+

(group 3), primary liver disease was not excluded in two, while one had diabetes, another diabetes and late latent syphilis, and the third a long history of peptic ulcer and questionable ulcerative colitis. Since controls were not obtained prior to treatment, the role of hydralazine as a causative agent in elevation of the cephalin-cholesterol flocculation value in these cases cannot be ascertained. In groups 2 and 3, 1 and 2+ flocculations were frequently found; they often reverted to normal after a short interval. Although the thymol turbidity of the serum became elevated with or prior to the cephalin-cholesterol flocculation, no significance can as yet be attributed to this test relative to this syndrome.

As reported by Hargraves,[3] fragmentary nuclei are usually found as a normal accompaniment of the L. E. preparation. The chromatin network of the nucleophagocytic cell undergoing a lysing process gradually becomes homogeneous, more and more resembling cells purported to be a step in the formation of the L. E. cell.[3] In this study, both phenomena were equally present in the positive and suspected cases (groups 1 and 2), lending support to the theory that transition from lysing nuclei to L. E. cell inclusion bodies may occur. If we accept the concept that the L. E. cell is dependent upon primary aberrations in serum globulin fractions, a rising cephalin-cholesterol flocculation value might well occur prior to the development of the L. E. cell as it did in this series. It is interesting that larger doses of hydralazine were required to control hypertension in the male, but the incidence of nucleophagocytosis and degenerated nuclei appeared to be higher in the female.

In order to gain more knowledge on the pathogenesis of collagen disease, a syndrome has been produced in eight dogs by the oral administration of hydralazine. Loss of weight, anorexia, weakness, aberrations in serum proteins, leukopenia, depression of plasma cholesterol, and development of the L. E. cell occurred.[4] Hydralazine may thus contribute to investigations of collagen disease.

The diagnosis of "hydralazine disease," however, is primarily a clinical one. A rising cephalin-cholesterol flocculation value is probably one of the earlier and more reliable laboratory tests when this diagnosis is suspected. Hydralazine is an extremely useful drug for the control of hypertension; the incidence of late toxic reactions is low enough to permit its use, especially in moderate-sized doses.

Summary and Conclusions

Two hundred thirty-six L. E. preparations were done on 105 hypertensive patients receiving various doses of hydralazine (Apresoline) hydrochloride for two weeks to four years. Ninety-seven patients were considered asymptomatic or were not suspected of hydralazine disease, and eight definitely exhibited the disorder. Of the 97, smears on 10 contained occasional or rare L. E. cells, but the numbers were insufficient to suggest a diagnosis of disseminated lupus erythematosus. It may be concluded from this series that the typical L. E. cell may appear, though rarely, in the blood of asymptomatic patients receiving hydralazine. In men, late toxic effects of hydralazine occurred in those receiving larger doses of the drug. The cephalin-cholesterol flocculation test may be 3 or 4+ shortly after the onset of symptoms, followed by the development of the L. E. cell phenomenon. Comparative studies suggest that nucleophagocytosis may precede the L. E. cell as an integral stage in its development.

Addendum

Since the submission of this manuscript, 4 of the 10 patients in group 2 have shown positive smears, with clinical and laboratory evidence of hydralazine disease.

600 S. Kingshighway (Dr. Schroeder).

1. (*a*) Morrow, J. D.; Schroeder, H. A., and Perry, H. M., Jr.: Studies on the Control of Hypertension by Hyphex: II. Toxic Reactions and Side Effects, Circulation **8**: 829, 1953. Dustan, H. P.; Taylor, R. D.; Corcoran, A. C., and Page, I. H.: (*b*) A Syndrome Elicited by Prolonged Administration of Large Doses of Hydralazine, abstracted, Proceedings of the 25th Annual Meeting of the Central Society for Clinical Research, J. Lab. & Clin. Med. **42**: 801, 1953; (*c*) Rheumatic and Febrile Syndrome During Prolonged Hydralazine Treatment, ibid. **154**: 23 (Jan. 2) 1954. (*d*) Perry, H. M., Jr., and Schroeder, H. A.: Syndrome Simulating Collagen Disease Caused by Hydralazine (Apresoline), J. A. M. A. **154**: 670 (Feb. 20) 1954. (*e*) Shackman, N. H.; Swiller, A. I., and Morrison, M.: Syndrome Simulating Acute Disseminated Lupus Erythematosus: Appearance After Hydralazine (Apresoline) Therapy, ibid. **155**: 1492 (Aug. 21) 1954. (*f*) Reinhardt, D. J., and Waldron, J. M.: Lupus Erythematosus-like Syndrome Complicating Hydralazine (Apresoline) Therapy, ibid. **155**: 1491 (Aug. 21) 1954.

2. Zimmer, F. E., and Hargraves, M. M.: The Effect of Blood Coagulation on L. E. Cell Formation, Proc. Staff Meet. Mayo Clin. **27**: 424, 1952.

3. Hargraves, M. M.: Systemic Lupus Erythematosus and L. E. Cell Phenomenon, Scientific Exhibit, Postgrad. Med. **16**: 163, 1954.

4. Comens, P.: Experimental Hydralazine Disease and Its Similarity to Disseminated Lupus Erythematosus, J. Lab. & Clin. Med., to be published.

IMPROVED NONCRUSHING CLAMP FOR USE IN GASTROENTEROLOGICAL OPERATIONS

William F. Rienhoff, M.D., Baltimore

In spite of the fact that there are many clamps available today that may be employed in surgical procedures on the stomach, small intestine, and large intestine, it is felt that the clamp described herein, a modification of some of its predecessors, is an improvement. It has been found to be most satisfactory, particularly in operations upon the stomach.

Some years ago an attempt was made to devise a clamp to be used on the stomach that would deliver an even pressure throughout the blade, eliminating the scissors-like action of most of the clamps in use. In the latter type, the blade near the handle received the greatest amount of pressure, whereas the tip of the clamp received the least. This often allowed the viscus to slip out unless additional support was given to the tip by some form of a supplementary adaptor placed on the ends of the clamp. Dr. Paul Banzet of Paris, France, devised a stomach clamp that is in use today. It was designed by the Gentile Instrument Company of Paris and is produced in France. An extended arm of the handle of this clamp is attached to the blade at an equal distance from both ends. The instrument is fragile; the blades are insecure and quite short.

With the aid of the instrument designer, Mr. Fred Todt, associated with Pilling & Company, an attempt was made

From Johns Hopkins University.

to make a better clamp, with the same idea of obtaining an equable distribution of pressure on the blade. Permission was granted by Dr. Banzet to use his original idea of attaching the handle of the clamp to the middle of the blade. Except for this point, however, the clamp herein reported differs radically from the original Banzet instrument. The blades of the clamp are narrow (fig. 1) and are lined with very fine teeth that eliminate the

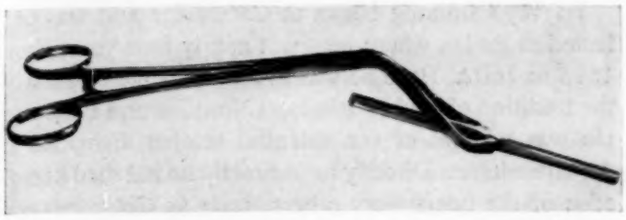


Fig. 1.—Newly designed clamp for use in surgery on the gastrointestinal tract and blood-vascular system.

necessity of using either rubber or gauze but still hold the viscus firmly without in any way crushing, devitalizing, or traumatizing the viscus. The teeth penetrate, very superficially, only the serosa and the outermost portion of the muscular coat. These teeth are similar to the teeth used in clamps for the ductus arteriosus and other blood vessels. In one jaw there are two rows, which set into three rows on the opposite jaw (fig. 2).

It is to be noted that the handle of the clamp is offset, so that only the even, or smooth, surfaces of the blades are in place, enabling unhindered continuous or interrupted suture of the tissue, which protrudes about 0.5 cm. beyond the blade. This instrument can be used for partial or total gastrectomy, on the esophagus, or on any part of the small or large intestine. In a subtotal gastrectomy, it enables the second assistant to hold the cut end of the stomach in a most favorable position for the operator to make the type of anastomosis that he prefers.

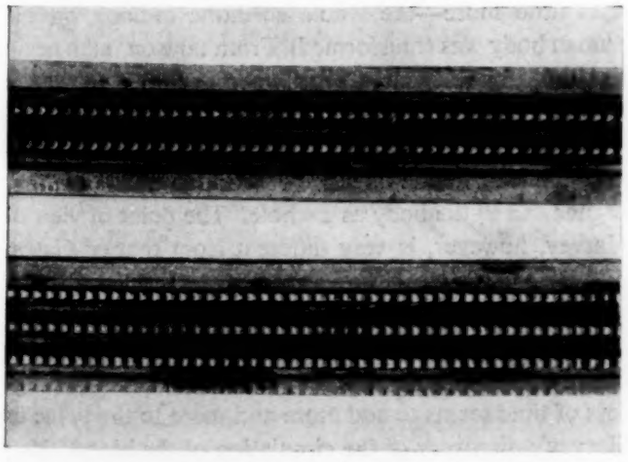


Fig. 2.—Jaws of clamp, showing rows of fine teeth.

The clamp is available in one long, straight model, two shorter models, or a long, curved model. Because of the stability of these clamps and the nontraumatic action, this type of instrument greatly facilitates operations on the gastrointestinal tract and can be used successfully in certain procedures on the blood-vascular system.

1201 N. Calvert St. (2).

SPECIAL ARTICLE

HARVEY AND MEDICAL RESEARCH

Louis N. Katz, M.D., Chicago

Ordinarily, public meetings are held for the laying of cornerstones, the unveiling of paintings and statues, or the dedication of memorials of many kinds. A meeting to commemorate the addition of a book to a library is indeed an uncommon reason for a gathering, especially when the book was first published over 300 years ago; however, the book the Chicago Heart Association is presenting to the John Crerar Library, on the library's 60th anniversary of service, is not just another book. It is William Harvey's book on circulation, which some have said is the most important book in medical history. In 1628 an event of international import took place: William Harvey, an Englishman, published the first Latin edition, "*Exercitationes de motu cordis et sanguinis,*" in Frankfurt, Germany, after years of study at Cambridge, England, capped by his sojourn at the great center of learning in Padua, Italy, where he had been thoroughly indoctrinated by its great medical leaders. A copy of this first Latin edition has been donated to the Crerar Library by Mr. Edward L. Ryerson. This book was translated into English, and in 1653 it first appeared as "The Anatomical Exercises . . . Concerning the Motion of the Heart and Blood." It was printed by Francis Leach, London, England, for Richard Lowdes. The Chicago Heart Association has procured a copy of the first edition of this English version and has given it to the John Crerar Library.

A voluntary health agency, the Chicago Heart Association, is making an unprecedented gesture by this gift to a privately endowed and publicly sustained library, a gift purchased from money voluntarily contributed by the public. Modern knowledge is dependent in great measure upon an adequate record of the past, because what we know today and what we will learn tomorrow is intricately linked with the stores of knowledge so painfully produced by our predecessors. This is true in every field but in none more so than in the field of research. It is not enough merely to accumulate these records of the past. These archives must be organized in such a way as to be readily available to the student of today and tomorrow. This is the role of a library. To me, therefore, this occasion represents first of all recognition of how important the historical written documents and journals in the files of the John Crerar Library are to

From the Department of Cardiovascular Research, Michael Reese Hospital.

An address, on the occasion of the presentation to the John Crerar Library by the Chicago Heart Association of a copy of the first English edition (1653) of William Harvey's book "The Anatomical Exercises Concerning the Motion of the Heart and Blood," Chicago, March 22, 1955.

Dr. Frederick Lendrum, University of Illinois; Mr. Herman H. Henkle, John Crerar Library; and Mrs. Edith Roberts, Chicago Heart Association, assisted in the literature research.

the city of Chicago in helping to make it a leading center of medical research. This occasion also gives us the opportunity to pay homage to William Harvey, one of the most illustrious predecessors in cardiology. It is not for me to attempt a historical review of cardiology, since this has been done by many others, such as the late Dr. James B. Herrick, who, in 1942, wrote a short history of cardiology.[1]

Harvey is but one name in the flow of great names rooted in antiquity and including some still living today. Who are we to judge the historical merit of contemporary work? We are much too close to it. And who are we to identify the sources of older knowledge simply from the writings of a few? Each of us is a product of his era, whether he be the unknown writer of the Edwin Smith papyrus of the 16th century B. C., who, as the late Dr. Walter W. Hamburger [2] pointed out, expressed the views of his period upon the pulse and circulation, or a Hippocrates of the 4th century B. C., or a Celsus of the first century A. D., a Galen of the 2nd, a Maimonides of the 12th, a Leonardo da Vinci, a Servetus, a Vesalius, or a Harvey of the 16th, or a Herrick of this day. Knowledge flows continuously, at times slowly, at other times with great rapidity. The work of Harvey was not an isolated fragment in the stream of history. It was part of that stream. Harvey knew that his own discoveries were founded on the work of others and that his work would serve as the basis for other discoveries still to come. In the first English edition of his book, he appended a communication to one of his critics that contained these wise words: "there is no science which has not its beginning from foregoing knowledge." [3] It would seem to me, therefore, that with these first editions of Harvey's books in our possession, and surrounded as we are by these exhibits of great medical works of the past, we should be more than commonly aware of that heritage called the past, more imbued than usual with a sense of history's unbroken stream and the part that this present generation can play therein.

Biographic Sketch of Harvey

Harvey lived from 1578 to 1658. His younger days were spent in the era of Queen Elizabeth and William Shakespeare. His life and career spanned the reigns of James I and Charles I, under both of whom he served as physician to the king. In the field of art, Rubens and Van Dyke were his contemporaries, as were Van Helmont the chemist, Napier the mathematician, Descartes the philosopher and mathematician, and Galileo and Kepler the astronomers. In the field of scientific medicine, Harvey was their peer. The year 1600 was an amazing year. In that year William Gilbert published "De Magnete," a book that is responsible (among many other things) for the word "electricity." In that year John Napier, who was constructing the first table of logarithms, (according to Glaisher [4]) made a mathematical invention that is unique in its usefulness and simplicity—he invented the decimal point. In that year (according to Sir Edmond Chambers [5]) Shakespeare's "Merchant of Venice" was first published and "Julius Caesar" and "Hamlet" were written, and William Harvey (according to a conversation recorded by Robert Boyle [6]) noted that the direction of the valves in veins tells a story that directly contradicts the dogma that had been unchallenged since the days of Aristotle and Galen. At that moment the modern conception of the circulation of the blood was born.

Harvey's training began at Cambridge and was perfected at Padua where he spent nearly four years, from 1598 to 1602. Here he was in an atmosphere rich with the tradition of such teachers as Vesalius and Fallopius. He was a pupil of the splendid teacher Fabricius of Aquapendente. Directly or indirectly he imbibed knowledge of the heart from others, such as Columbus and Cesalpino. He returned to England, engaged in private practice, was physician to St. Bartholomew's Hospital, and made investigations particularly in the field of embryology (some of which he began at Oxford), in comparative anatomy, and in the physiology of the circulation. Many of his views concerning this latter subject were set forth in his lectures at the College of Physicians, and these were collected and published in Latin. This great master lived to the age of 79 and enjoyed the gratification of overcoming all existing opposition. It was only a few years after his death that his concepts were confirmed with the discovery of the capillary circulation by Malpighi, who had the advantage of the invention of the microscope by Leeuwenhoek.

Meaning of Harvey's Work

The importance of Harvey's book was expressed by Charles Singer in "The Evolution of Anatomy," when he wrote: "Harvey's great work . . . appeared . . . as a miserably printed little quarto. By this brief tract—for it is little more—the whole scientific outlook on the human body was transformed. From now on, men begin to think physiologically even when occupied in purely anatomical study. . . . With Harvey, at last, a clear idea again emerges that each organ has a discoverable function and is related in its mode of working to all the other organs and to the body as a whole. The point of view of Harvey, however, is very different from that of Galen, and in the coming centuries we hear less of Design and more of the Machine." [7] Like all great discoveries, once established, they seem so obvious. Sir T. Lauder Brunton expressed this thought best when he said: "The progress of time seems to add more and more to the value of Harvey's discovery of the circulation of the blood. Yet, when you read his simple statement of how he made his discovery, you wonder why it had not been made before. It occurred to him, he said, that the blood might go round, as it were, in a circle. The discovery is almost childlike in its extreme simplicity, and yet it is the basis of all the exact knowledge of the processes of life which we possess today, and of all the power to prevent death which knowledge affords us." [8]

Being an investigator myself, I find Harvey's work represents a major revolution in research, the recognition of the importance of the two complementary facets of observation and experiment. Claude Bernard, the father of physiology, writes that "medicine is still pursuing a scientific solution to the problem [of conserving health and curing disease], which has confronted it from the first. . . . During its advance through the centuries, however, medicine has always been driven into action and from numberless ventures in the realm of empiricism has gained useful information. Though furrowed and overturned by all manner of systems so evanescent that, one by one, they have disappeared, it has none the less carried on research, acquired ideas and piled up precious materials which in due time will find their place and meaning in scientific medicine. . . . Thanks to the great development and powerful support of the physicochemical sciences, study of the phenomena of life, both normal and pathological, has made progress which continues with surprising rapidity." [9] And he continues further: "Only within very narrow boundaries can man observe the phenomena which surround him; most of them naturally escape his senses, and mere observation is not enough. To extend his knowledge, he has had to increase the power of his organs by means of special appliances; at the same time he has equipped himself with various instruments enabling him to penetrate inside of bodies, to dissociate them and to study their hidden parts. A necessary order may thus be established among the different processes of investigation or research, whether simple or complex: The first apply to those objects easiest to examine, for which our senses suffice; the second bring within our observation, by various means, objects and phenomena which would otherwise remain unknown to us forever, because in their natural state they are beyond our range. Investigation, now simple, again equipped and perfected, is therefore destined to make us discover and note the more or less hidden phenomena which surround us."

Present Trend in Medical Research

"In the philosophic sense, observation shows, and experiment teaches." [10] I have quoted Claude Bernard at length because he gives a perfect description of Harvey's contribution, and these passages explain why Harvey is properly called the father of the modern experimental approach to medicine. Now, I wonder what Harvey would say were he to come upon the present scene of medical research with its splendid great advances, with its elaborate equipment, with its public acclaim, and with knowledge rolling from the laboratories not only through scientific journals but through all the mediums of public information. Would Harvey's impression be the same as mine? I recall that when I started out in my research career 35 years ago, medical research was a career limited in financial opportunity, in public awareness, and in popularity. It was considered a career that only those with strong compulsions—and strong constitutions—would enter; it was far more to the point to go into practice. After all, full-time careers in medicine were few and far between. How different things are today. Positions for full-time medical men are plentiful in medical schools, in universities, in government, and in industry. There are positions not only for teachers, health officers, and administrators but for investigators as well. Even in the hospitals, whether public or private and university or nonuniversity, the full-time positions are expanding. The demand far exceeds the supply. Obviously, with such a trend, the quality of personnel will go down, especially in the preclinical branches and in the basic sciences of biology where young men are first inspired. How can the basic sciences compete with the clinical departments, with government, and with private industry? And yet it is in the basic sciences that the best men are needed.

With the recent increase in opportunities, the feeling has grown that everyone who undertakes a full-time position in academic work must also do research. In fact, it is getting to the point where every practicing physician thinks he must do research. Production in research is becoming one of the most common measures of a man's ability and right to advance. Sometimes this measure is weighted by the number of papers written and not by their quality. New appointments are sometimes made by colleagues unfamiliar with the applicant's special field of study. Hence, one may hear reasoning to the effect that Dr. A. wrote 50 papers while Dr. B. wrote only 3 and so Dr. A. must be better. Dr. A.'s board, benefactors, and public will all be duly impressed by such an output, and consequently there shall be a bigger institution, a larger budget, and increased endowment. Bigness is becoming confused with goodness. Alas, today too many judge institutions by their size rather than by the attainments of their scholars. Yet today, more than ever before, the desperate need is for scholars. Worse still, research men work in a fishbowl today. Their reports are avidly inspected by the lay press, radio, television, and magazines. It is tempting to hit the headlines, and some succumb. Others are helpless victims of publicity both because the public-relations counsel of their institution feels compelled constantly to "feed hand-outs" to the fourth estate and because, with millions of dollars in taxes and contributions pouring into research, the government and the voluntary health agencies feel it necessary to "sell the public." And the product they sell is the work of the defenseless investigator. One wonders what Harvey, if he were to return today, would make of all this ballyhoo. Would he seek the headlines?

Dignity of Research.—Research is a dignified profession to be pursued only by the consecrated and inspired, in quietude, at a leisurely pace, and away from prying eyes. It cannot be placed on a business footing where one new fact is to be returned for each quantum of dollars invested. I have actually heard some persons propose to set up a committee to find out what needs to be done in discovering a cure for some specified malady. I have heard them suggest gathering all the eminent scientists together and putting them to work so that the cure will come in their lifetime. Of course these individuals, worried about themselves, would like to hurry the process. Since industry has been successful by harnessing men together, the uninitiated naturally believe that research

results can be accomplished in the same way. Unfortunately this is not necessarily so. Great discoveries are not produced on the assembly line. Only duplicates can be so manufactured. The original must come about through the deliberate activity of a creative mind. And a creative mind works best away from artifices and prodding. Great discoveries evolve—they are not delivered on call. This was the case with Harvey. The public should utilize its energies to help recruit the creative minds, to prepare the proper climate for their work in terms of space, equipment, assistants, funds, and social acceptance, and then sit back and patiently await results. And results will be forthcoming, as they have been in an ever-increasing stream during the last few decades.

Types of Research.—Research is not of one pattern. There are many kinds of research approaches, and I suppose all types are necessary. Some research is plodding, like Ehrlich's discovery of arsphenamine. One drug after another is tried, or one test is painfully used, and then another and another. After many failures comes success. This kind of research is scarcely appealing. Then, there is intuitive research—a minimum of perspiration and a maximum of inspiration, as it were. The danger lies in going off in the wrong direction. There are so-called investigators who make universal truths from flimsy evidence. These are the ones who find a correlation of limited extent and immediately report an axiom. As a result, a great deal of work must then be done by others to disprove their extensive deductions. This does not mean that theory or hypothesis has no value in research. All investigators worthy of the name have concepts before they start to experiment, but this is merely to lend direction to their work. They keep their beliefs to themselves until they have tested them over and over again. Then, and then only, will they talk or write about them. One must distinguish the true investigator from the philosopher who does just a few experiments so that he may write a paper to sound off his preconceived notions. The medical literature abounds in such "half-baked" studies. Often the facts are sound, but the interpretation is obviously illogical.

The best research, I believe, is the kind where the investigator asks a simple question and designs his study in such a way as to get from it a yes or no answer. This was Harvey's way. Nothing is so gratifying as a clear 'yes' in such a planned study. Even a clear 'no' is helpful, since the investigator can set up another experiment designed to get a yes or no answer to the next question that follows logically upon the first. This view of research is often lost sight of by the uninitiated who set up their investigation to prove something. Research is not meant to prove anything. It is meant to find the truth. This does not mean that the investigator has no hunch. It does mean that he is constantly checking his beliefs and is ready to alter or discard them if the investigations fail to support them. This is the "test by fire" of the real investigator. Some of the great discoveries come by accident, but they require a trained observer to appreciate their significance and to be ready to shift his line of work when fortune smiles upon him in this way. It is the possibility of such accidental discoveries that makes it proper to have large groups of trained investigators constantly at work in important areas. For only to the prepared mind is the accidental discovery significant, and only he can perceive and make use of it. This is why we must cherish and encourage trained investigators.

Comment

One of the hazards of expanding knowledge is specialization. More and more becomes known about less and less. There is a need to reverse this trend in medicine and in science. With specialization there develops a specialized technical language that is incomprehensible to the uninitiated. Knowledge becomes compartmentalized. Important information may be overlooked on that account. There is need of interdisciplinary cross fertilization. This is one of the vital reasons for medical centers and research teams. Departmental barriers should be easily passed, and a research followed wheresoever it leads, regardless of the disciplines or the tools employed. Medical research men are manufacturers of new knowledge made ready for the physician to dispense to his patient, the ultimate consumer. Without the manufacture of such new knowledge, the physician is handicapped and is limited to the products now available. It must be appreciated that in many plants new manufacture cannot begin until new tools are available. These new tools come from special plants. In research, the creating of new tools is known as basic research. Basic research may arise in the chemistry or physics laboratory, in biology, zoology, or botany, in microbiology, in embryology, in physiology, in anthropology, in psychology, in mathematics, in epidemiology, and in other strange and exotic places. Once these basic research tools are created, they can be applied to developmental research for diagnostic procedures, therapeutic approaches, and prophylaxis. It must not be forgotten that the Manhattan project, important as it was in developing atomic bombs, was a development based on some views created by a few brilliant theoretical physicists. Antibiotics were developed during the war after a bacteriologist named Fleming accidentally discovered a clearing on an agar culture. It is obvious that research will flourish only as long as basic research flourishes. Once basic research dies out, the rest of research will wither on the vine.

Research is not done only in the laboratory. It may be conducted at the bedside, in the operating room, and in the field of public health and epidemiology. It is not the place that counts. It is the perspective. It is the original mind asking a question and designing an experiment to find the answer. It should not be pebble picking—it should be the building of magnificent castles. I have no sympathy for the view that any kind of research is good. Research should advance a fundamental concept or it should have an obvious practical value and early application. Research is not gadgeteering. It is the pursuit of ideas. With the development of elaborate tools, like flame photometers, ultracentrifuges, angiocardiographs, ballistocardiographs, electron microscopes, electrophoresis, and isotopes, there has developed a small group who play their instruments for all they are worth. Having acquired the equipment, the buildings, the technicians, and the project grants, they go madly searching for ideas. They scrutinize grant applications if they are on research-allocation committees, they scan published

reports, they rush to meetings, they write to their friends, and they ask visiting colleagues for ideas. This is obviously all wrong. Research should start from ideas, and then tools should be obtained, not vice versa. Unfortunately, the other has developed because in certain quarters it is considered fashionable to have elaborate equipment. It takes a Szent-Györgyi to get great results with only a frog-heart, a simple lever, and an old-fashioned smoked drum—and a creative mind. He is one of the many modern prototypes of Harvey, working quietly in many laboratories. Research to some so-called investigators is like fashion. They follow the popular fields and shift as the fashion changes. A leader starts a new line of study, all the so-called *re*seachers quickly follow. Fortunately, their number is small. We do not need many *re*searchers; what we need today are searchers. My instinct is to work away from the popular field. One can follow one's bent better. There is no rush to finish, consequently a better and more thorough study will result, which gets the accolade that counts from one's peers. This satisfaction is second to none.

Recently a regrettable trend has developed in support of research—the project grant. How can any sensible investigator outline what his work is going to be and predict where it will lead over the course of the next year or two? Research is not that simple. It cannot be compartmentalized in short-term packages. Therefore, it usually follows that the project-grant application is looked upon as just a form, filled out to obtain support for a major undertaking to cover many years and leading who knows where. All who have seriously considered this problem admit that the project grant is a makeshift. But no better device has yet been developed to take its place. Besides supporting research plants or institutions of learning we should above all support men and women. We should train novices with the compulsion to do research and the capacity to be our future teachers, clinical leaders, and investigators. We should support established investigators on the basis of past performance and future promise, without compelling them to fit into the tight corset of a project application. We should support teams of investigators in like manner. We should make all good investigators feel that support will be forthcoming for long periods of time if they are deserving. Only in this way will we continue to maintain a crop of dedicated investigators who can concentrate on their research and thereby continue to manufacture the new products so necessary for the practicing physician to meet the needs of his patients, so vital to cure disease, and, ultimately, to eliminate and prevent it.

Summary

Research is a gratifying career, and those in it are rather exclusive. Only those dedicated to it are wanted to join the ranks. Those in research believe that progress has been made in knowledge and that research has justified itself. They do not wish this wonderful profession spoiled by amateurs and opportunists. Not everyone is suitable for a career in research. But if the compulsion to become an investigator is overwhelming despite dissuasion, come on and join in. The career gives pleasure and satisfaction. There are many dedicated investigators in the medical sciences. Harvey would be satisfied were he here today, with their motivation and with their accomplishments. It seems only a short time ago, a matter of only some 50 years, when this tremendous explosion of new knowledge first appeared on the horizon. All of us are familiar with the great advances in the cardiovascular field, the new diagnostic tools, the new surgical operations, the new antibiotics, the new hormones of the adrenal, pituitary, and sex glands, and the increasing role of radioisotopes in diagnosis and therapy. Hope is the new watchword in medicine today. It has put fear in the background, and nowhere is this truer than in regard to diseases of the heart and blood vessels. This is all due to the investigators and to the public support of research. It is something in which all can take great pride. For as the great physician Sir William Osler so aptly said in "Aequanimitas": "The great possession of any University is its great names. It is not the 'pride, pomp, and circumstance' of an institution which brings honor, nor its wealth, nor the number of its schools, nor the students who throng its halls, but the men who have trodden in its service the thorny road through toil . . . to the serene abode of Fame." [11] This is the lesson to be derived from William Harvey's life and work. For Harvey was one of the world's clearest thinkers and observers—a man who defied tradition and the unquestioning acceptance of authority, a man who abhorred dogma and believed more in a posteriori reasoning than in a priori speculation. William Harvey deservedly is the father of modern experimental medicine, and he truly walked the thorny road through toil to the serene abode of fame.

29th Street and Ellis Avenue (16).

1. Herrick, J. B.: A Short History of Cardiology, Springfield, Ill., Charles C Thomas, Publisher, 1942.
2. Hamburger, W. W.: Earliest Known Reference to Heart and Circulation: Edwin Smith Surgical Papyrus, Circa 3,000 B.C., Am. Heart J. **17**: 259-274, 1939.
3. Harvey, W.: The Anatomical Exercises Concerning the Motion of the Heart and Blood, London, England, F. Leach, 1653.
4. Glaisher, J. W. L., in The Napier Tercentenary Memorial Volume, edited by C. G. Knott, New York, Longmans, Green & Co., Inc., 1915.
5. Chambers, E.: Shakespeare: A Survey, London, England, Oxford University Press, 1926.
6. Franklin, K. J.: Valves in Veins: An Historical Survey, Proc. Roy. Soc. Med. (Sect. History Med.) **21**: 1-33, 1927.
7. Singer, C.: Evolution of Anatomy: A Short History of Anatomical and Physiological Discovery to Harvey, New York, Alfred A. Knopf, Inc., 1925.
8. Brunton, T. L.: Collected Papers on Circulation and Respiration, London, Macmillan & Co., Ltd., 1906-1916, vol. 1, 2nd series, pp. 567-568.
9. Bernard, C.: Introduction to the Study of Experimental Medicine, New York, the Macmillan Company, 1927, p. 1.
10. Bernard,[9] p. 5.
11. Osler, W.: Aequanimitas with Other Addresses, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1932, p. 9.

Radioactive Iodine Therapy.—Some of the outstanding advantages of I^{131} therapy in Graves's disease are: (1) Mortality is zero. It is possible that a patient with impending crisis may be precipitated into a state of active thyroid crisis because of thyroid-gland breakdown following treatment. . . . It is possible that in a rare instance inadequate therapy, by postponing control, might permit cardiac decompensation to become fatal. This, however, is much more likely to occur in nodular goiter than in Graves's disease. (2) There is no cord paralysis. (3) There is no permanent tetany; one example of post-I^{131} tetany of a temporary type is reported in the literature. (4) Control is complete in almost 100% of patients. (5) Thyroid size usually is reduced to nearly normal. (6) There is no discomfort. (7) There is no disability from treatment and usually no time lost from work. (8) Recurrence is almost unknown. (9) Recurrence, if present, can be safely and effectively treated with additional I^{131}.—E. P. McCullagh, M.D., On the Choice of Treatment for Hyperthyroidism, *Annals of Internal Medicine*, February, 1956.

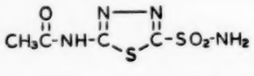
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs that appear in this column have been authorized by the Council for publication and inclusion in New and Nonofficial Remedies. They are based upon the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary.*

Acetazolamide.—5-Acetamido-1,3,4-thiadiazole-2-sulfonamide.—The structural formula of acetazolamide may be represented as follows:



Actions and Uses.—Acetazolamide, a heterocyclic sulfonamide compound, is a potent inhibitor of carbonic anhydrase, the enzyme that catalyzes the reversible hydration of carbon dioxide and dehydration of carbonic acid. The most important pharmacological action of acetazolamide is referable to inhibition of carbonic anhydrase in the renal tubule resulting in a depression of tubular reabsorption of bicarbonate; however, the drug acts in a manner completely different from that of the organic mercurials, promoting the excretion of bicarbonate ion rather than chloride ion. The result of this selective action is loss from the extracellular fluid, by way of the kidney, of sodium bicarbonate, to a lesser extent of potassium bicarbonate, and of an isosmotic equivalent of water. Thus, diuresis, alkalinization of the urine, and a mild degree of metabolic acidosis occur.

Acetazolamide is absorbed rapidly from the gastrointestinal tract. Peak plasma levels are reached within 2 hours after administration, and the duration of therapeutic effectiveness is about 8 to 12 hours. The drug is rapidly excreted in an unchanged form by the kidney, about 80% of a single oral dose appearing in the urine within 8 to 12 hours.

Acetazolamide has been employed as a diuretic in the treatment of edema associated with congestive heart failure. Unlike most mercurials, it is well tolerated when given by the oral route, but its diuretic action is not as rapid or as dramatic as that observed after organic mercurial therapy. Patients with predominantly left-sided decompensation severe enough to require hospitalization usually do not respond well to therapy with this agent. In these patients, mobilization of pulmonary edema fluid is best achieved by use of the mercurials; however, subsequent replacement with acetazolamide may often maintain such patients in an edema-free state, with relief from dyspnea and orthopnea. In patients with severe right-sided heart failure and large accumulations of fluid, paracentesis is generally required before favorable responses to acetazolamide can be elicited. Here too, it is frequently necessary to initiate diuretic therapy with the mercurials, with subsequent replacement by acetazolamide.

The best results with this drug have been obtained in ambulatory patients with mild to moderate cardiac decompensation and cor pulmonale. Its use does not eliminate the need for other therapy such as with digitalis, bed rest, fluid restriction, or sodium-free diet. It is of no value in the treatment of nephrotic edema or nephritis.

Acetazolamide has been employed in the treatment of epilepsy. It is not known whether beneficial effects result from the systemic acidosis that the drug produces or from direct inhibition of brain carbonic anhydrase. Preliminary clinical investigations indicate that administration of the drug, alone or in conjunction with other therapy, is moderately successful in controlling seizures in selected cases of petit mal and grand mal epilepsy refractory to other forms of therapy. Since the response to the drug is inconsistent, it is difficult to determine which patients will respond favorably to therapy; therefore, its ultimate usefulness in the treatment of this condition remains to be determined.

Acetazolamide appears to have therapeutic value in the treatment of glaucoma. Its action is different from that of the usual miotics, since the drug depresses the formation of the aqueous humor rather than facilitates its drainage; it is therefore most valuable as a supplement to the therapy with cholinergics generally used to reduce intraocular pressure. The effects of prolonged therapy with acetazolamide are not conclusive, and long-term therapy requires careful selection of patients and careful observation while they are receiving the drug. With short-term therapy, the drug has proved useful in reducing intraocular pressure in patients in whom the standard miotics have been unsuccessful. In severe acute cases, acetazolamide is particularly helpful in permitting the ophthalmologist to temporize and to evaluate the situation more carefully before undertaking surgery.

Undesirable side-effects of acetazolamide therapy, though rather frequent, are usually not serious and are rapidly reversible. Drowsiness and paresthesias over the face and extremities are the most commonly encountered side-effects. Fatigue, excitement, gastrointestinal upsets, and polydipsia have been observed less frequently. In patients with hepatic cirrhosis, the drug may induce episodes of disorientation. Since acetazolamide is rapidly excreted, the inhibition of carbonic anhydrase by daily oral doses is intermittent, and compensatory mechanisms prevent serious distortions of acid-base balance; however, it is contraindicated in idiopathic renal hyperchloremic acidosis. Because the drug causes a sodium and potassium diuresis, it is also contraindicated in all conditions in which there is a known depletion of these ions, including adrenal cortical hypofunction (Addison's disease) or all types of adrenal failure. Since acetazolamide is a sulfonamide derivative, it is possible that any of the untoward reactions reported after bacteriostatic sulfonamide administration could occur after acetazolamide therapy. Fever and allergic type skin eruptions have already been reported in patients receiving this drug. Although other manifestations of sulfonamide reactions such as bone marrow depression, crystalluria, and renal calculi

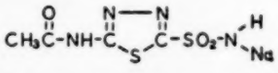
have not been observed, the physician should be alert for the appearance of such reactions, and the drug should be withdrawn at the first sign of their occurrence.

Dosage.—Acetazolamide is administered orally. For diuresis in patients with congestive heart failure, 0.25 to 0.375 gm. daily in the morning appears to be the optimal dosage, although some may respond to administration every other day. Increasing the dosage beyond this level does not increase the diuresis and may increase the incidence of side-reactions. If diminished diuretic effectiveness occurs after prolonged administration, dosage adjustments may be necessary. In the treatment of epilepsy, the dosage must be individualized according to the response of the patient. Although some patients are reported to respond to lower doses, the proposed range is 0.375 to 1 gm. once a day. If the drug is administered adjunctively with other anticonvulsants, the initial daily dose should not exceed 0.25 gm. This can then be increased gradually. In the treatment of acute congestive and secondary glaucoma, acetazolamide should be used as an adjunct to the usual miotic therapy in doses of 0.25 gm. every 4 hours.

Preparations for use as stated for the foregoing drug are marketed under the following name: Diamox.

Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of acetazolamide.

Acetazolamide Sodium.—Sodium 5-acetamido-1,3,4-thiadiazole-2-sulfonamide.—The structural formula of acetazolamide sodium may be represented as follows:



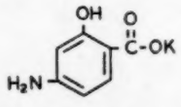
Actions and Uses.—Acetazolamide sodium, the sodium salt of acetazolamide, exhibits the same actions and has the same potency as equivalent amounts of acetazolamide. It is more soluble than the parent drug and may therefore be administered parenterally. (See the monograph on acetazolamide.)

Dosage.—Acetazolamide sodium is administered by either the intramuscular or intravenous routes. It should be given only when oral administration of acetazolamide is impractical. The dosage, expressed in terms of the parent drug, is the same as for acetazolamide. (See the monograph on acetazolamide.)

Preparations for use as stated for the foregoing drug are marketed under the following name: Diamox Sodium.

Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of acetazolamide sodium.

Potassium Aminosalicylate.—The potassium salt of aminosalicylic acid.—The structural formula of potassium aminosalicylate may be represented as follows:



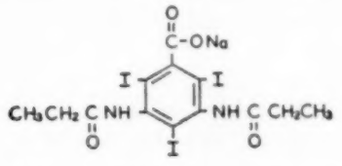
Actions and Uses.—Potassium aminosalicylate shares the action and use of the parent drug, aminosalicylic acid, and its other salts in the chemotherapy of tuberculosis. (See the monograph on aminosalicylic acid in New and Nonofficial Remedies.) There is some evidence that the potassium salt may cause less gastric intolerance than the acid or sodium salt. It can be used in place of the sodium salt for patients required to restrict their sodium intake, but otherwise is subject to the same precautions and side-effects.

Dosage.—Potassium aminosalicylate is administered orally. The average dosage for adults is 12 gm. daily in three or four divided doses.

Preparations for use as stated for the foregoing drug are marketed under the following names: Paskalium; Paskate.

Glenwood Laboratories, Inc. and Eli Lilly & Company cooperated by furnishing scientific data to aid in the evaluation of potassium aminosalicylate.

Sodium Diprotrizoate.—Sodium 3,5-dipropionamido-2,4,6-triiodobenzoate.—The structural formula of sodium diprotrizoate may be represented as follows:



Actions and Uses.—Sodium diprotrizoate is employed as a contrast medium for intravenous (excretory) urography. The drug is transported rapidly to the kidneys and accumulates in the urine shortly after administration. For this reason, roentgenographic exposures are best made 5, 10, and 15 minutes after intravenous injection. When excretion is delayed by impaired renal function, it may be necessary to wait 30 minutes or longer before adequate roentgenographic shadows can be obtained. The density of the shadows is also influenced by the plasma iodine content and the concentration of the urine at the time of examination; thus, careful timing of exposures and restriction of preexamination fluid intake is necessary for satisfactory pyelograms.

Side-effects of sodium diprotrizoate are similar to those produced by other contrast media of this type. Chief among these are nausea and vomiting, sweating and sense of intense warmth, urticaria, and pain in the injected arm. Serious cardiovascular side-effects are uncommon. The incidence of all types of reactions has been reported by various investigators to be between 10 and 15%. (See the general statement on water-soluble organic iodine compounds for roentgenography in New and Nonofficial Remedies.)

Dosage.—For excretory urography, 20 to 30 cc. of a 50% solution is the usual intravenous dose for adults. A slow rate of injection (3 to 4 minutes) has been observed to decrease the incidence of side-effects. Before the full amount is injected, a "test dose" of about 1 cc. should be administered intravenously and the patient observed for signs of untoward reactions. Since aqueous solutions of sodium diprotrizoate are photosensitive, the drug should not be used after prolonged exposure to daylight.

Preparations for use as stated for the foregoing drug are marketed under the following name: Miokon Sodium.

Mallinckrodt Chemical Works cooperated by furnishing scientific data to aid in the evaluation of sodium diprotrizoate.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

Editor and Managing Publisher . . AUSTIN SMITH, M.D.
Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
Editor for Medical Literature Abstracts . GEORGE HALPERIN, M.D.
Assistant Editor . . . . . WAYNE G. BRANDSTADT, M.D.

Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

POTENTIAL VALUES OF THE AUTOPSY TODAY

GUEST EDITORIAL

Isaac Starr, M.D.

For at least a generation, medicine was dominated by the great pathological school. During this era, American students flocked to the German universities, especially to Vienna, where the emperor had decreed that everyone dying in the General Hospital should have an autopsy, a great advantage over the American hospitals, where permission from the family of the deceased was required, and often refused. Osler, the leader of this school in the United States, was so successful in academic medicine that his type of training, that of a gross pathologist, was widely copied. When I was a student, every professor of medicine occupying an important chair in America had had extensive autopsy experience. In those days, the autopsy room was the center of the hospital's research activities, and the privilege of doing the autopsies was much sought after. The chiefs gathered there, and the clinicopathological conference was considered the last word in undergraduate teaching. As a young man, I was advised that, if I wanted to get anywhere in academic medicine, I must perform at least 100 autopsies myself.

From the vantage point of another medical generation, it is interesting to assess the strength and weakness of the pathological school. Their strength lay in their stern insistence on demonstrable facts, facts so plain that all were forced to agree. Who could deny the presence of a gastric ulcer when the stomach was passed around; one could put one's finger in it. In the face of realism of this kind, a host of medical vagaries were swept away, such as those of a clinical professor in my school who is reported to have asked the students to learn the symptoms characteristic of 14 types of gastric neuroses.

In therapeutics, the adherents of the pathological school either were nihilists or were strongly influenced by that line of thought. How could a reasonable man expect to heal the lesions found at autopsy? Dr. Richard Cabot used to teach that, of the 562 diseases known to man, 4 could be cured and 5 more alleviated. I may not have the figures right, but I have the spirit exactly right. Osler is reported to have said—surely with a twinkle in his eye, because he had the greatest sense of fun imaginable—that if anyone was admitted to his service at the Johns Hopkins Hospital, he could assure them of a most careful physical examination and a scrupulously careful autopsy. Doubtless this therapeutic skepticism aided in sweeping away the polypharmacy and the trust in a host of illogical remedies characteristic of the earlier medical generation, but no positive advances in therapeutics derived from this school. Also, the aspects of medical practice not found at autopsy not only were of no interest to these doctors but were likely to be dismissed as imaginary or nonexistent. Thus, the attitude toward emotional disorders was that there was nothing really the matter, even though the patient might be altogether incapacitated for useful work and a burden to himself and his family. And in the concern with the terminal features of disease, interest in prevention was at a low ebb. Finally, the members of this school were content with the description of what they saw; experiment was alien to almost all of them.

The present era contrasts very greatly with that which preceded it. It is characterized by increasing reliance on experiment as a means of acquiring medical knowledge, by increasing interest in the functional aspects of disease, and, since these are often susceptible to treatment in a way anatomic lesions are not, by great advances in therapeutics. With this changing emphasis, interest in the autopsy has declined, and what has happened in my own school seems typical of what is taking place throughout the United States, although in most places the change has not progressed so far.

As the pathological era drew near to an end, the professor of pathology in my university changed with the times and became interested in experimenting. Soon the behavior of neoplasms in experimental animals began to absorb his attention, and his interest in the autopsies waned steadily. As time passed, it became harder and harder for him to find young men interested in performing the routine autopsies. To make matters worse, the general population, acquiring greater regard for the medical profession and an increasing interest in medical research because of the therapeutic triumphs of recent years, became more and more willing to allow autopsies to be performed on their near relatives. At the Massachusetts General Hospital, where as an intern in 1921 I struggled to obtain autopsies, we considered ourselves doing well when we secured such permission in 30% of our deaths; at present, in most teaching hospitals this value approaches 90%. Also, in this period, the beds in the University Hospital almost doubled and the deaths increased correspondingly.

So, at present, the morgue is swamped with routine work. What used to be a rare privilege has become a burden. The keenness, audacity, and mental caliber of the personnel performing the autopsies have declined greatly from the levels of the previous generation, and the autopsies are not nearly as well done as formerly. They are still being done much the same way as they were by Virchow and Rokitansky; it is hard to think of any other branch of medicine that has been so static for so long.

From the Hospital of the University of Pennsylvania, Philadelphia.

What may be called the creative imagination is altogether lacking. What wonder the clinical professors do not gather around any longer.

If any research of importance is coming from studies being made at routine autopsies at present, I am not aware of it. Doubtless, an occasional rarity still needs to be reported, but who would advise a promising young clinician, or indeed a pathologist, to spend much time doing autopsies today? What wonder that the new professor of pathology in my school, an expert experimenter, has washed his hands of the whole business and has declined to be responsible for the routine autopsy service any longer, a step certainly to the advantage of his important experiments on neoplasms. But, as far as the autopsies themselves are concerned, things seem to be at the nadir.

Autopsies will always be of value to the profession. They are of great importance in the teaching of medical students and nurses. They permit clinicians to test their acumen in the diagnosis of anatomic lesions, often at a cost to their pride, but with great gain in their wisdom. They instruct surgeons in the end-results of their work. In other words, they are invaluable to the profession. Careful thought must be given to the problem of their decline. I have certain suggestions to make.

In the first place, the old way of doing autopsies has gone on too long. Huge stacks of records and files of cards have been accumulated, apparently with the hope and expectation that someone would someday dig into the mass of material and come up with gold nuggets of valuable information. But in recent years no one has and, in my opinion, no one will. It seems ridiculous to continue gathering routine information of this kind when so much remains undigested. The type of autopsy performed should change.

Certainly the routine could be greatly simplified, the aim being restricted to securing information of immediate utility to the clinicians in charge of the case. In such case, microscopic sections would be cut only rarely, and then only under the direction of some person with a special interest, which would guarantee that the effort would not go to waste. Perhaps the autopsies would be better performed by the physicians and surgeons personally interested in the cases, as in the old days. Surely the routine autopsy would not then lack clinical interest, and I doubt if it would be done less skillfully than at present. We also need to expand the interest in other directions than the anatomic. Our knowledge of the chemical pathology of the blood might not benefit from the autopsy, but the chemical pathology of diseased organs is a field just beginning to be explored, and its extent is limitless.

My own experience points to still another type of solution. Several years ago, I was driven to the morgue for much the same reason that drove so many from the clinic to animal experiments in the past; by simulating systole in cadavers, one could make important measurements concerned with the heart and circulation with an accuracy not possible either in the clinic or in experimental animal preparations.[1] Thus, with work accurately measured, a search for clinical methods of estimating the heart's work was possible. Ample blood for perfusion experiments was found to be available from bottles discarded by the blood bank as unfit for use in the living. The experiments were difficult, but one had the *élan* that comes with pioneering. They became easier as we gained experience.

The number of experiments that could be done on autopsy material is limitless, and many would give results of immediate importance to clinical medicine. Why be content with the description of an abnormal artery when one could determine the resistance to the flow of blood through it and the pressure that caused rupture? One can envision direct tests of the function of heart valves and of the degree of stenosis. Surgeons could experiment with new techniques to diminish regurgitation through diseased valves and to widen stenosis, and they could assess their immediate results by direct measurement before and after. One way to bring back interest to the morgue in this experimental era is to perform experiments there. There is no lack of opportunity for one with imagination.

COMMISSION ON CHRONIC ILLNESS

In the January 28 issue of THE JOURNAL is an editorial on the termination of the activities of the Commission on Chronic Illness. This body, which was founded in 1949 by the American Hospital Association, the American Medical Association, the American Public Health Association, and the American Public Welfare Association, will terminate its activities as an incorporated organization in June, 1956. However, at least some of its projects will be continued under the auspices of the sponsoring agencies.

Elsewhere in this issue of THE JOURNAL (page 1114) is a discussion that was presented at the last meeting of the Commission on Chronic Illness. It summarizes the progress in prevention of chronic illness from 1949 to 1956 and provides an excellent picture of the problem today. There are probably few subjects that are of greater importance and that are receiving more consideration than chronic illness. The subject poses a real challenge to the medical profession and others interested in health and promises to be of increasing importance as the average age of the population increases.

---

1. Starr, I.; Horwitz, O.; Mayock, R. L., and Krumbhaar, E. B.: Standardization of the Ballistocardiogram by Simulation of the Heart's Function at Necropsy: With a Clinical Method for the Estimation of Cardiac Strength and Normal Standards for It, Circulation **1**: 1073-1096 (May) 1950. Starr, I.; Schnabel, T. G., Jr., and Mayock, R. L.: Studies Made by Simulating Systole at Necropsy: II. Experiments on the Relation of Cardiac and Peripheral Factors to the Genesis of the Pulse Wave and the Ballistocardiogram, ibid **8**: 44-61 (July) 1953. Starr, I., and Schnabel, T. G., Jr.: Studies Made by Simulating Systole at Necropsy: III. On the Genesis of the Systolic Waves of the Ballistocardiogram, J. Clin. Invest. **33**: 10-22 (Jan.) 1954. Starr, I.; Schnabel, T. G., Jr.; Askovitz, S. I., and Schild, A.: Studies Made by Simulating Systole at Necropsy: IV. On the Relation Between Pulse Pressure and Cardiac Stroke Volume, Leading to a Clinical Method of Estimating Cardiac Output from Blood Pressure and Age, Circulation **9**: 648-663 (May) 1954. Starr, I., and Schnabel, T. G., Jr.: Studies Made by Simulating Systole at Necropsy: V. Estimation of the Contour of the Left Ventricular Ejection Curve by an Adjusted Integration of the Aortic Blood Pressure Curve, J. Appl. Physiol. **7**: 273-278 (Nov.) 1954. Starr, I.: Studies Made by Simulating Systole at Necropsy: VI. Estimation of Cardiac Stroke Volume from the Ballistocardiogram, J. Appl. Physiol. **8**: 315-329 (Nov.) 1955. Starr, I.; Askovitz, S. I.; Feder, W., and Schild, A.: Studies Made by Simulating Systole at Necropsy: VII. Clinical Methods for Estimating the Work of the Left Ventricle, with a Note on the Diminution of Heart Work as Age Advances, Circulation **12**: 1005-1021 (Dec.) 1955.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

I am thoroughly convinced that whenever controversies exist it is much better for all parties concerned to put their cards face up on the conference table at the earliest possible moment. Then rumor can be faced with facts, and smoldering resentment can be replaced with good will. Such an attitude is imperative if we wish to have universal support for medical education by the physicians through the American Medical Education Foundation. There is no room for misunderstanding, suspicion, or criticism.

Medical education in the United States has advanced by leaps and bounds since my days in medical school. The American Medical Association was organized in 1847 for the express purpose of improving medical education as it then existed. In 1904, an investigation of the problems connected therewith was carefully studied by a commission headed by Flexner. The report, now known as the Flexner report, revealed that many of our medical schools were not satisfactory institutions. The report made all of us sit up and take notice, and, as a result, many of the schools that were found to be inefficient either closed their doors or amalgamated with other schools, so that in a short time most of the remaining institutions were classed as meeting the minimum requirements recommended in the report. This was the rebirth of medical education. Today all of the medical schools are approved—there are 82 of them, and some new ones are in various stages of development. Medical education is one of our proudest achievements. A man or woman graduating today, with an internship or residency from one of our approved hospitals, is eminently qualified to practice medicine.

Each school has an admissions committee whose sole job is to screen the applicants for admission to the freshman class. The American Medical Association has no voice in this selection, its sole interest being that the school meets the requirements for approved classification. The purpose of the school is to train men and women to care for the ill. This, of course, implies extensive research and health programs, which are necessary to produce the well-educated physician. All of this costs a great deal of money, and every medical school is always looking for more funds, which are essential to keep each school at the peak of its efficiency. About half of our schools are classified as private, while the other half are state or municipally supported. Careful surveys, however, have shown that all of our schools receive liberal contributions from tax monies and, for this reason, have much in common. The cost of medical education varies from $3,000 to $4,000 a year per student. The students pay about one-fifth of this cost as tuition. The balance must be obtained from some other source.

Many teachers are, for the most part, inadequately paid because of lack of funds, and, as a result, techniques have been developed in different localities for the direct purpose of caring for this problem. I happen to know that these techniques have caused criticism in certain areas. It does seem that troubles are increased when finances are involved. To help solve some of these problems, the National Fund for Medical Education was established to solicit funds from business and industry and the American Medical Association formed the American Medical Education Foundation to solicit financial help from the profession. I have spoken for this fund many times, and afterwards I have been asked questions by both physicians and laymen that I have been personally unable to answer. Some of the questioners, as a result of real or fancied grievances, were very vocal. Many of the objections of the practicing physicians to the schools have to do with techniques employed to increase the incomes of the full-time teachers. I am personally convinced that all of these various controversies are solvable at the local level, if both the teachers and the practitioners—most of whom in both groups are represented in the state medical associations and the school authorities—would get together and discuss their mutual problems. I believe that every question I have been asked is solvable under the code of ethics of the American Medical Association. The educators need the practitioners, and the practitioners need the educators; neither is an independent entity. The American physician will support medical education financially and voluntarily, but a lot of present misunderstandings must be discussed over the conference table.

I, personally, have had no experience with these problems. I believe that every physician owes something to his own medical school. I would also like to see every physician in America contribute to the American Medical Education Foundation, so that every school could have sufficient funds to do the best possible job. I know that business and industry will do their fair share if we do ours. Our difficulties are not insurmountable, but their solution requires frank and open discussion around the conference table. Once the educator and the practitioner meet and freely discuss and solve real or fancied problems, the atmosphere will become clearer and the financial support of medical education by the physicians of America will be astonishing.

I wholeheartedly favor every physician supporting medical education by contributing to the American Medical Education Foundation.

ELMER HESS, M.D., Erie, Pa.

ORGANIZATION SECTION

INVESTMENT ADVISOR FOR A. M. A.

The Board of Trustees has approved the selection, by the A. M. A. Finance Committee, of Security Supervisors, a Chicago firm, to advise the Association on the use of its investment fund. The firm's location makes it possible for its counselors to familiarize themselves with any changes in fund requirements and to maintain a close personal contact with A. M. A. headquarters. A counselor will recommend basic policy to the Finance Committee; associates will then draft recommendations to the Secretary and will handle operational details in cooperation with the Comptroller. Security Supervisors, which was organized in 1930, today is a six-man partnership plus staff. Client's accounts have assets estimated in excess of 250 million dollars.

ADVISORY COMMITTEE ON TELEVISION AND MOTION PICTURES

The American Medical Association has formed a Physicians' Advisory Committee for television, radio, and motion pictures. Physicians, serving on both the Los Angeles and New York committees, will assist network script supervisors, producers, and writers in the preparation of television and radio programs on medical subjects to assure technical accuracy of medical information disseminated to the public. This new project supplements the same type of service that has been carried on in the past through the office of Dr. W. W. Bauer, Director of the A. M. A. Bureau of Health Education.

The committees in both cities, where network television and radio production is centered, will provide three types of service: (1) checking of routine medical facts, (2) reviewing of complete scripts, and (3) providing on-the-set technical medical advisors during production of a TV or radio program. In Los Angeles, requests for technical assistance will be referred to Dr. Robert W. Gentry, Chairman, 1925 Wilshire Blvd., Los Angeles 57, and the New York contact is Dr. Gerald D. Dorman, Chairman, 51 Madison Ave., New York 10. Besides Dr. Gentry, the Los Angeles committee will be made up of Drs. E. Vincent Askey, A. M. A. Speaker of the House of Delegates, James F. Regan, William D. Evans, Eugene F. Hoffman, Richard O. Myers, Ian G. MacDonald, Dudley M. Cobb Jr., and Edward T. Tyler. In New York, besides Dr. Dorman, the committee will consist of Drs. Henry I. Fineberg and Renato J. Azzari.

Reviewing of complete scripts will be handled by the committees as a whole. If major revisions are necessary, the committees will meet in consultation with the writer. If physicians are needed to serve as technical advisors on the set or in radio or television studios, they will be appointed by the respective committees. Any producer desiring to use the name of the A. M. A. in connection with a program will be bound by the "Guiding Principles for Participation in Telecasts and Broadcasts" as adopted by the Board of Trustees.

A. M. A. GRANTS-IN-AID FOR RESEARCH

The Committee on Research of the A. M. A. announces that grants of $500 or less for clinical investigation are available and that applications should be filed by April 14. Grants will be made also for basic medical science research, but no more than two grants will be made in either field at any one school. These funds are not intended for the payment of salaries, secretarial help, technical assistance, or labor, and no overhead may be applied against them. The funds are limited for the purchase of drugs, chemicals, supplies, experimental animals, and equipment. They are intended to supplement grants from other sources.

Applications should contain a description of the proposed research and should be endorsed by an authorized official of the university. Applications should indicate the source and extent of grants from other agencies. Six copies, including the original, of the application should be submitted. Application blanks are available by writing to the Secretary, Committee on Research, American Medical Association, 535 N. Dearborn St., Chicago 10.

APPOINT NEW EDITOR OF STANDARD NOMENCLATURE OF DISEASES AND OPERATIONS

The Board of Trustees of the American Medical Association has appointed Dr. Edward T. Thompson as Editor of Standard Nomenclature of Diseases and Operations to succeed Dr. Richard J. Plunkett, who has been appointed associate director of the Joint Commission on Mental Illness and Health, with headquarters in Boston. Dr. Thompson has been a member of the Editorial Advisory Board of Standard Nomenclature for several years and is co-author of "Textbook and Guide to the Standard Nomenclature of Diseases and Operations." He is now chief of the program operations branch of the division of hospital and medical facilities of the U. S. Public Health Surveys in Washington, D. C.

NETWORK TELEVISION SHOWS

Three "March of Medicine" programs, presented by Smith, Kline & French Laboratories and the American Medical Association, will be aired over the NBC-TV network this spring. A report on geriatrics, featuring clinical work at Jackson Memorial Hospital, Miami, Fla., and the health education program at St. Petersburg, Fla., will be presented late in March. A topic has not been selected as yet for the May program. The final show in the 1956 spring series will feature the A. M. A. Annual Meeting in Chicago during the week of June 11.

MEDICAL NEWS

CONNECTICUT

Symposium on Cardiovascular Disease.—An all-day symposium on cardiovascular disease will be sponsored by the Stamford Heart Association April 5 at the Connecticut Power Company Auditorium, 429 Atlantic St., Stamford. Dr. William H. Resnik of Yale University School of Medicine, New Haven, will preside over the following program:

Edward F. Bland, Boston, Some Special Features of Rheumatic Heart Disease from a Long-Term Perspective.
M. Irene Ferrer, New York City, Selection of Patients for Mitral Commissurotomy.
Dwight E. Harken, Boston, Aortic and Mitral Stenosis and Insufficiency.
David Scherf, New York City, Mechanism of Origin of Arrhythmias.
Victor A. McKusick, Baltimore, Selected Aspects of Pericardial Disease.
William Dock, Brooklyn, Aneurysms and Aortic Insufficiency.
Henry T. Bahnson, Baltimore, Surgery of the Aorta and Great Vessels.

All physicians are welcome. Emergency calls will be received at Fireside 8-6411, Ext. 237. There is no registration fee.

ILLINOIS

Psychiatric Lectures.—Dr. Leo H. Bartemeier, medical director, Seton Institute, Baltimore, and clinical professor of psychiatry, Georgetown University School of Medicine, Washington, D. C., will present "The Management of Overeating, Overdrinking and Oversmoking" April 4, 8 p. m., at the North Shore Health Resort, 225 Sheridan Rd., Winnetka. Physicians are invited.

Public Health Conference.—The 16th annual conference of the Illinois Public Health Association will be held at the Hotel St. Nicholas, Springfield, April 5-6. After the address of welcome by Dr. Roland R. Cross, director, Illinois Department of Public Health, Springfield, "Public Health Approaches to the Problem of Aging" will be presented by Dr. Arnold B. Kurlander, medical director, Chronic Disease Program, U. S. Public Health Service, Washington, D. C., who will consider the somatic aspects, and Robert J. Havighurst, Ph.D., professor of education, University of Chicago, who will deal with the mental aspects. Panel discussions have been scheduled on "The Role of Public Health in the Detection and Prevention of Chronic Diseases," "Meeting the Aging Problem in Illinois," and "Sanitation and Suburban Development."

Chicago

Hektoen Memorial Lecture.—The third Ludvig Hektoen Memorial Lecture, originally scheduled for Feb. 23, was postponed in respect to the memory of Dr. Bruno Epstein, an intern at Cook County Hospital, who was killed in line of duty. The lecture "Our Daily Blood" was delivered by Dr. John G. Gibson II, research associate in medicine, Harvard Medical School, Boston, on March 8.

Dr. Molander Retires as Department Head.—Dr. Edward E. Gordon, medical director of the Institute for the Crippled and Disabled in New York since 1952, has been appointed director of the department of physical medicine at Michael Reese Medical Center to replace Dr. Charles O. Molander, who is retiring after 25 years as head of the department. Dr. Gordon has served as associate professor of rehabilitation medicine at the Columbia University College of Physicians and Surgeons, New York, and as consultant in the department of physical medicine at Roosevelt Hospital and the Manhattan Veterans Administration Hospital. Dr. Molander was recently made associate professor emeritus of physical medicine at Northwestern University Medical School.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

INDIANA

Postgraduate Programs.—The Indiana University School of Medicine, Bloomington-Indianapolis, announces a series of postgraduate programs, designed for both the specialist and the physician in general practice. The postgraduate series, approved for credit by the American Academy of General Practice under category 1, includes the following programs in April and May:

April 4, Cerebral Palsy: Etiology, diagnosis, treatment and end-result studies, encompassing neuropathology, neurology, neurosurgery, pediatrics, and orthopedics.
April 11, The Anemias: Diagnosis and treatment of various types; special problems as related to surgery, obstetrics, pediatrics, and other fields. Limited to 20.
April 18, Trauma: Basic principles and recent developments in surgical management; emergency surgical treatment of vascular, abdominal, and nervous system injuries.
May 21-22, Clinical Cardiology: Rheumatic heart and arteriosclerotic heart disease; basic concepts as background for modern diagnosis and treatment.
May 23, Lung Disease and Pulmonary Function: Commonly performed pulmonary tests, emphasizing the value in explanation of pathological physiology in common chest diseases.

MARYLAND

Pediatric Seminar.—Dr. J. Edmund Bradley, professor of pediatrics, announces the fifth annual Pediatric Seminar at Gordon Wilson Hall, University of Maryland Hospital, Baltimore, April 8, 10 a. m.-5 p. m. The following program will be presented:

Pediatric-Roentgenologic Problems, Edward B. D. Neuhauser, radiologist-in-chief, associate clinical professor in radiology, Harvard Medical School, Boston.
Recent Developments in Treatment of Infectious Diseases, Horace L. Hodes, director, department of pediatrics, Mount Sinai Hospital, New York City.
The Practitioner and Hematologic Diseases of Infants, Irving J. Wolman, associate professor of pediatrics, University of Pennsylvania School of Medicine, Philadelphia.
Urologic Problems Frequently Encountered in Children, Meredith F. Campbell, professor of urology, emeritus, New York University College of Medicine, New York City.

A banquet will be held for the guests and former residents the same evening at the Southern Hotel in Baltimore.

MASSACHUSETTS

Meetings of School Physicians.—The Massachusetts School Physicians' Association has scheduled a series of programs on Wednesdays at 2 p. m. "A Mental Health Center," with presentation of cases, will be the subject considered April 4 at the South Shore Guidance Center, 1120 Hancock St., Quincy, where Dr. Bellenden R. Hutcheson, Boston, director, will be in charge. "Physically Handicapped Children" will be discussed April 11 at the Massachusetts Hospital School in Canton. Dr. John Carroll, superintendent, will be in charge. On April 18 and 25 "The Responsibilities of School Physicians to Mentally Retarded Children" and presentation of cases will concern the meetings at the Walter E. Fernald State School in Waverly (Dr. Malcolm J. Farrell, superintendent, in charge).

MICHIGAN

Symposium on Office Procedures.—The Michigan Academy of General Practice will hold its third Symposium on Office Procedures at the Pantlind Hotel, Grand Rapids, April 4. Five category 1 credit hours will be granted. Panel discussion will follow the morning and afternoon sessions. A complimentary luncheon and cocktail reception are scheduled. Lederle Laboratories will be co-sponsor.

MISSOURI

Alumni Meeting.—The annual St. Louis City Hospital Alumni Association meeting will be held April 9 at LeChoteau Restaurant, St. Louis, in conjunction with the Missouri State Medical Association meeting. All former interns, residents, and staff members are invited to attend. For reservations write Dr. Drennan Bailey, Secretary, 634 N. Grand, St. Louis 3.

State Medical Meeting in St. Louis.—The 98th annual session of the Missouri State Medical Association will convene at the Sheraton-Jefferson Hotel, St. Louis, April 8-11, under the presidency of Dr. Victor B. Buhler, Kansas City. Four symposiums have been scheduled, each with an out-of-state speaker, as follows: Symposium on Surgery (Management of Severe Metabolic Deficits in the Surgical Patient, Dr. William D. Holden, Cleveland); Symposium on Pediatrics (Kidney Disease in Children, Dr. Henry L. Barnett, New York); Symposium on Medicine (Treatment of Patients with Coronary Atherosclerosis, Dr. E. Sterling Nichol, Miami, Fla.); Symposium on Obstetrics (Functional Uterine Bleeding, Dr. Leonard H. Biskind, Cleveland). Presentations by other out-of-state speakers will include:

Strengthening the Nutritional Processes During Aging, Tom D. Spies, Birmingham, Ala.
Victories or Victims: A Critique of Advances in Anemia, Claude Starr Wright, Augusta, Ga.
The Adequacy of Medical Education, Melvin A. Casberg, Solvang, Calif.
Renal Vicissitudes, T. Leon Howard, Denver.
Advances in Surgery of the Pancreas, Herbert C. Lee, Richmond, Va.

A panel on acute surgical emergencies will be presented Tuesday at 4 p. m. and a panel, "What's New in Medicine?" Wednesday at 10 a. m. Dr. Buhler will preside at the annual banquet in honor of past presidents, Tuesday, 7:30 p. m., at which Elmer Ellis, Ph.D., president of the University of Missouri, Columbia, will have as his subject "What the University of Missouri Medical School Should Mean to the State."

NEW JERSEY

Hospital News.—The Atlantic City Hospital will have as visiting chiefs pro tem. Dr. Eugene P. Pendergrass, professor of radiology, University of Pennsylvania School of Medicine, Philadelphia, April 2-6; Dr. Harold J. Jeghers, professor of medicine and director of the department, Georgetown University School of Medicine, Washington, D. C., April 9-13; Dr. Charles H. Best, professor of physiology, Banting and Best Department of Medical Research, University of Toronto (Canada), April 16-20; Dr. Seymour J. Gray, assistant professor of medicine, Harvard Medical School, Boston, April 23-27; and Dr. Edwin E. Osgood, professor of medicine and head of the division of experimental medicine, University of Oregon Medical School, Portland, April 30-May 4.

NEW YORK

Sesquicentennial Celebration.—The Broome County Medical Society will celebrate its 150th anniversary April 4 with a dinner at the Arlington Hotel, Binghamton, where Dr. Elmer Hess, Erie, Pa., President of the American Medical Association, and Dr. Renato J. Azzari, New York City, president of the Medical Society of the State of New York, will address physicians of the county and their wives. Honored guests of the medical society include widows of all deceased physicians who now reside in the county, presidents of the county medical societies in the sixth district, Medical Society of the State of New York, and local government officials.

Oto-Ophthalmologic Session.—The Brooklyn Eye and Ear Hospital Alumni Association will hold its fifth annual scientific session at the Brooklyn Eye and Ear Hospital April 7. Speakers on ophthalmology will be Drs. Ralph I. Lloyd, Brooklyn; Willis S. Knighton, New York City; Harold G. Scheie, Philadelphia; and Daniel Kravitz, Brooklyn. There will be a motion picture symposium on the following topics: "Surgical Treatment of Glaucoma: Goniotomy and Goniopuncture in Treatment of Congenital Glaucoma" by Dr. Scheie and "Cataract in Glaucoma" (loaned through the courtesy of Dr. Wendell L. Hughes, Hempstead). Otolaryngological subjects will be presented by Drs. Philip E. Meltzer, Boston; N. Lagoumis and Salmon C. Harvey, Brooklyn; Lyndon A. Peer, Newark, N. J.; and Irvin J. Fine, Perth Amboy, N. J.

Conference on Tuberculosis.—The annual conference of the New York Tuberculosis and Health Association, April 3, at the Hotel Statler will have as its theme "A New Look at Tuberculosis Prevention." The all-day open session will consider such questions as "Where Are We Today in TB Prevention?" "What About Nutrition and Problems of Housing Related to TB?" and "What's New in Preventing Transfer of Infection from the Sick to the Well?" Dr. Foster Murray, Brooklyn, president, will preside at the luncheon at 12:45 p. m., which will be addressed by John J. Theobald, deputy mayor of the city of New York. Dr. Hans Abeles, assistant director, bureau of tuberculosis, New York City Department of Health, and Dr. Byard Williams, New York City, chairman, committee on housing, Community Service Society, will participate in the morning program on housing and health. Dr. Thomas N. Sheen, New York City, chairman, annual conference program committee, will preside over the following afternoon program, which will be devoted to progress reports in tuberculosis prevention:

Improving Nonspecific Resistance: Clues from Nutrition Research, Joseph A. Johnston, Detroit.
Specific Approaches to the Prevention of Tuberculosis, Robert L. Price, Washington, D. C.
Modern Methods of Reducing Transfer of Infection, Arthur B. Robins, New York City.

New York City

Lecture on Neoplastic Diseases.—On April 6 at 3 p. m. "Exfoliative Cytology of Uterus and Breast with Emphasis on the Diagnosis of Early Malignant Lesions" will be discussed by Dr. George N. Papanicolaou, professor emeritus, Cornell University Medical College, and director of the Papanicolaou Research Laboratory, in the West Basement Conference Hall at Montefiore Hospital.

Conference on Mercury and Its Compounds.—A Conference on Mercury and Its Compounds will be presented by the New York Academy of Sciences, section of physics and chemistry and section on biology, April 6 and 7, at the Barbizon-Plaza Hotel, 101 W. 58th Street at Sixth Avenue. Friday morning will be devoted to physics and chemistry, Friday afternoon to pharmacology and toxicology, and Saturday morning to clinical medicine. Dr. Harry Gold, Cornell University Medical College, will serve as chairman for the Saturday session, which will include:

Mechanism of Action of Mercurial Diuretics in Man, Raymond E. Weston, New York.
Mercurial Diuretics and Electrolytes, William B. Schwartz, Boston.
Bioassay of Organomercurials, Theodore H. Greiner, New York.
Clinical Effectiveness of Mercurial Diuretics in Congestive Heart Failure, John M. Evans, Washington, D. C.
Outpatient Management of the Cardiac Patient with Oral Mercurial Diuretics, William E. Lawrence and Margaret E. S. Klapper, Birmingham, Ala.
Mercurial Diuretics—A Long-Term Evaluation, George C. Griffith, Los Angeles.
Special Problems of Management of Patients on Mercurial Diuretic Therapy, Emanuel Goldberger, New York.
Mercurial Diuretics in Toxemia of Pregnancy and Other Clinical Indications, James W. Hendrick, Jacksonville, Fla.

Attendance is limited to those invited to participate in these conferences and to interested members of the academy.

OHIO

Friedlander Lecture.—At a joint meeting of the Academy of Medicine of Cincinnati and the Heart Council, April 3, the Friedlander Lecture, "Some Cardiac Disorders Amenable to Surgical Treatment," will be presented by Dr. Helen Brooke Taussig, associate professor of pediatrics, Johns Hopkins University School of Medicine, and physician-in-charge, Cardiac Clinic, Harriet Lane Home, Johns Hopkins Hospital, Baltimore.

TENNESSEE

State Medical Meeting in Memphis.—The 121st annual meeting of the Tennessee State Medical Association will convene at the Hotel Peabody, Memphis, April 8-11, under the presidency of Dr. Charles C. Trabue IV, Nashville. General scientific sessions are scheduled for the morning and meetings of specialty societies for the afternoon. The meeting will open Monday at 9 a. m. with a movie, "Cancer of the Thyroid." The Monday morning session will close with a symposium, "Anesthesia and Anesthetic Agents," moderated by Dr. Ray G. Stark, Memphis. The Tuesday morning session will conclude with a symposium, "Present Day Treatment of Pulmonary Tuberculosis," for which Dr. W. Walton Hubbard, Nashville, will serve as moderator. A panel discussion on the use and abuse of antibiotics is

scheduled for 11:10 a. m. Wednesday. The meeting of the Tennessee Society of Pathologists will open Monday, 1:30 p. m., with "Aspects of the Experimental Pathology of Choline—Deficient States" by Dr. W. Stanley Hartroft, St. Louis. For its meeting Monday afternoon, the Tennessee Academy of General Practice has scheduled a symposium on peripheral vascular disease. The Tennessee State Pediatric Society will hold its meeting Monday afternoon at LeBonheur Children's Hospital Amphitheatre, where "Some Current Problems in Antibiotic Therapy" by Dr. John P. McGovern, New Orleans, will be followed by "Recent Advances in Nutrition of Children" by Dr. Robert L. Jackson, Columbia, Mo. The Tennessee chapter, American College of Surgeons, will hear Dr. James H. Semans, Durham, N. C., discuss "Trauma of the Genito-Urinary Tract" Tuesday, 2:30 p. m. The Tennessee Radiological Society will present an open scientific session Tuesday afternoon, at which "Mediastinal Masses" by Dr. Ted F. Leigh, Emory University, Ga., will precede a diagnostic film-reading panel. On the same afternoon the Tennessee Diabetes Association will have a symposium on vascular disease in diabetes. At its dinner, 6:30 p. m., the guest speaker, Dr. Elliot V. Newman, Nashville, will have as his subject "Fluid and Electrolyte Balance in Endocrine Disease." The meeting of the Tennessee Heart Association will open after a luncheon, 1 p. m., with "Certain Aspects of Myocardial Anoxia" by Dr. Richard J. Bing, Birmingham, Ala. The woman's auxiliary to the Tennessee State Medical Association will meet simultaneously with the parent body and is invited to attend the President's Night Banquet Monday, 7 p. m., at which Dr. F. J. L. Blasingame, Wharton, Texas, will discuss "Organized Medicine and Its Role in America." Dr. Blasingame is a member of the Board of Trustees of the American Medical Association and a past-president of the Texas Medical Association.

TEXAS

Annual Tumor Conference.—The fifth annual State Tumor Conference will be held April 4 in Wichita Falls. After explanation of "Importance and Aims of Wichita County Medical Society Tumor Clinic" by Dr. Bailey R. Collins, Wichita Falls, Dr. Edward A. Gall, University of Cincinnati College of Medicine, Cincinnati, will speak on "Carcinoma as Lesion of Multicentric Origin" and "Clinical and Pathologic Manifestations of Malignant Lymphoma." The "Role of Radiotherapy in Management of Breast Cancer" and "Diagnosis and Treatment of Neuroblastoma" will be discussed by Dr. William B. Seaman, Washington University School of Medicine, St. Louis, and "Clinical Evaluation of Compartmental Fluid Shifts" and "Observations on Histochemistry of Thyroiditis," by Dr. Champ Lyons, Medical College of Alabama, Birmingham. In addition to the scientific program, there will be a combined luncheon meeting with the Thirteenth District Medical Society, at which the speaker will be Dr. Milford O. Rouse, Dallas, president-elect of the Texas Medical Association.

VIRGINIA

Phi Delta Epsilon Lectureship.—The Alpha Mu chapter of the Phi Delta Epsilon Fraternity at the Medical College of Virginia, Richmond, will hold its sixth annual lectureship April 3 at 12 noon in the George Ben Johnson Auditorium of the medical college. The guest speaker, Dr. William Parson, chief of medicine, University of Virginia School of Medicine, Charlottesville, will discuss "Obesity."

Medical Lectures at the University.—In its spring series of evening medical lectures, the University of Virginia, Charlottesville, will present the following programs in the auditorium of the medical school at 8 p. m.:

April 5, Harold L. Stephen, University of Liverpool, Liverpool, England, Hypopituitarism.

April 9, James H. Leathem, Ph.D., Rutgers University, Problems in Infertility (Nu Sigma Nu Lectureship).

April 16, Charles M. Pomerat, Ph.D., University of Texas Medical Branch, Galveston, Tissue Culture in Experimental Biology and Medicine (Phi Chi Lectureship).

April 23, A. Stone Freedberg, Beth Israel Hospital, Boston, Thyroid Function in Health and Disease; Recent Advances and Their Therapeutic Implications (Phi Lambda Kappa Lectureship).

WASHINGTON

Surgical Meeting in Spokane.—Dr. H. Glen Bell, professor of surgery, University of California Medical School, San Francisco, will be guest speaker at the annual session of the Spokane Surgical Society, April 7, at the Davenport Hotel in Spokane.

Meeting of Obstetricians.—The spring meeting of the Washington State Obstetrical Association will be held at the Washington Athletic Club, Seattle, April 7. Dr. Robert A. Kimbrough of the University of Pennsylvania School of Medicine, Philadelphia, will present "Treatment of Carcinoma of the Cervix with End Results" and "Changing Indications for Caesarean Section." Dr. John I. Brewer of Northwestern University Medical School, Chicago, will discuss "Indications for Hysterectomy and Indications for Oophorectomy" and "Menstruation and Its Disorders." Dr. Russell R. deAlvarez of the University of Washington School of Medicine, Seattle, will be moderator. In the evening a panel discussion on medicolegal aspects of obstetrics and gynecology will be held by Judge Eugene Wright of King County Superior Court, Mr. Edward L. Rosling, counsel for the Washington State Medical Association, Mr. John Warme of Aetna Casualty Company, and Dr. James H. Berge, Seattle, president-elect of the Washington State Medical Association and chairman of the medical disciplinary board.

WEST VIRGINIA

Society News.—Two brothers recently completed terms as president of component medical societies in West Virginia, serving simultaneously during 1955. Dr. J. A. Kyle Bush of Philippi has served as president of the Barbour-Randolph-Tucker Medical Society and his brother, Dr. Ivan H. Bush Jr., of Oak Hill, as president of the Fayette County Medical Society.——A joint committee has been named by the West Virginia State Bar and the West Virginia State Medical Association to study the advisability of the development of an "Interprofessional Code" between the two groups. The medical group consists of Drs. Walter E. Vest, Huntington, chairman, James S. Klumpp, Huntington, Sobisca S. Hall, Clarksburg, Frank J. Holroyd, Princeton, and Russell Kessel, Charleston, all past-presidents of the West Virginia State Medical Association.——At a meeting of the section on neurology, neurosurgery, and psychiatry of the West Virginia State Medical Association at Weston State Hospital in Weston, on the afternoon of April 7, Dr. David C. Wilson, professor of psychiatry and neurology, University of Virginia School of Medicine, Charlottesville, will discuss "The Psychiatrists's Role in Cultural Changes." Dr. Hiram W. Davis, superintendent of Huntington State Hospital, will preside. Dr. H. Sinclair Tait, superintendent of Weston State Hospital, will be host at a social hour and buffet supper. An invitation to attend has been extended to all physicians in West Virginia. Those who expect to be present are requested to notify Dr. Tait.

WISCONSIN

Orthopedic Field Clinics.—The Bureau for Handicapped Children, state department of public instruction, announces the following schedule for orthopedic field clinics in April: Superior, April 5-6; Sheboygan, April 11-12; Marinette, April 18; and La Crosse, April 24-27. The clinics are conducted for persons under 21 years of age who are referred by their family physician for orthopedic diagnosis and consultation. Forms for referral may be obtained from the Bureau for Handicapped Children, 146 North, State Capitol, Madison 2.

ALASKA

Named Commissioner of Health.—Dr. Charles R. Hayman, Juneau, deputy commissioner of health since 1954, has been named acting commissioner of the Alaska Department of Health, to serve the two remaining years of the term of Dr. C. Earl Albrecht. The latter resigned after 10 years as Alaska's first full-time commissioner of health to become assistant director of the Ohio Department of Mental Hygiene and Correction in Columbus (THE JOURNAL, Feb. 11, page 490).

GENERAL

Meeting of Physicians and Surgeons.—The annual meeting of the Association of American Physicians and Surgeons will be held at the Deshler-Hilton Hotel, Columbus, Ohio, April 5-7, under the presidency of Dr. James L. Doenges, Anderson, Ind. The banquet speaker, Clarence Manion, J.D., former dean of the law school, Notre Dame University, South Bend, Ind., will have as his subject "The Way Back to Freedom." Among the speakers will be Dr. Charles L. Hudson, Cleveland, president, Ohio State Medical Association, Dr. Edward W. Harris, president, Columbus (Ohio) Academy of Medicine, and Dr. Edward R. Annis, Miami, Fla., whose topic will be "To Socialized Medicine and Socialism Through the Complacency of Physicians."

Microcirculatory Conference.—The third Microcirculatory Conference for Physiology and Pathology will be held April 3 in conjunction with the American Association of Anatomists at the Schroeder Hotel, Milwaukee. The theme of the conference, "Regulation of Blood Flow," will be developed in the following morning program:

Interrelation of Physical and Physiological Factors in the Microcirculation, Alan C. Burton, Ph.D., department of biophysics, University of Western Ontario Faculty of Medicine, London, Ontario, Canada.
Smooth Muscle of Small Blood Vessels, Brenton R. Lutz, Ph.D., Melrose, Mass., and George P. Fulton, Ph.D., department of biology, Boston University.
Pharmacological Factors in Relation to the Cardiovascular System, Edward D. Freis, Veterans Administration Hospital, Washington, D. C.

After luncheon a panel symposium, "Microcirculation in Tissues and Organs," will be presented. A social period, 6:30 p. m., will precede dinner.

Course on Tissue Culture.—The Tissue Culture Association will sponsor a course of instruction in the principles and techniques of cell and tissue culture at the University of Colorado School of Medicine, Denver, July 16-Aug. 11 (tuition, $100). The course, which will be under the direction of Charles M. Pomerat, Ph.D., University of Texas Medical Branch, Galveston, "is designed to give to responsible investigators a background of general information on cultured cells and an opening wedge of training in the application of the method to problems in several current areas of research." It is planned specifically for postgraduates (M.D. or Ph.D.) who intend to use cultured tissues in their research or teaching. Requests for application forms should be addressed to Mary S. Parshley, Ph.D., College of Physicians and Surgeons, 630 W. 168th St., New York 32, and should be completed and returned to her not later than May 1. Successful candidates will be notified about May 15.

World Health Day.—World Health Day, April 7, will have as its theme "Destroy Disease-Carrying Insects!" The special day is promoted by the World Health Organization, which has as its goal: ". . . the attainment by all peoples of the highest possible level of health. . . ." In his message for World Health Day, Dr. Fred L. Soper, director of the Pan American Sanitary Bureau, Regional Office of the World Health Organization, in Washington, D. C., points out that "For ages man has accepted insects as an unavoidable curse and many people still think of them more as a nuisance than as one of man's deadliest enemies. Only within the past half century has their role as disease carriers been firmly established. Until recent years their control was costly, geographically restricted—and not too effective. Today the picture has changed radically, with the development of residual insecticides such as DDT, which remains effective for at least six months. This has made possible the concept of eradication, one of the most important developments in public health history. . . ."

Kimble Methodology Research Award.—Nominations for the fifth Kimble Methodology Research award are being accepted until June 1. This award, which gives recognition to the application of scientific knowledge to the Public Health Laboratory, was established by the Kimble Glass Company of Toledo, Ohio, and is sponsored by the Conference of State and Provincial Public Health Laboratory Directors. The entry should be either (1) a fundamental contribution that serves as a base line for development of diagnostic methods that fall within the province of the public health laboratory or (2) the adaptation of a fundamental contribution to make it of use in a diagnostic laboratory. The work should have been completed within the preceding five years and should be accompanied by a reprint or a summary with bibliography and a statement of the considerations that justified the recommendations of the study. Nominations received after June 1 will be considered for nomination in 1957, providing the work was completed since Jan. 1, 1951. Nominations should be sent to Thomas S. Hosty, Ph.D., Bureau of Laboratories, Alabama State Department of Health, Montgomery 4. An award of $1,000 and a silver plaque will be presented at the annual meeting of the conference in Atlantic City, N. J., next November.

Blood Bank Institute.—A blood bank institute and workshop for medical technologists in Catholic hospitals will be offered at Georgetown University, Washington, D. C., April 2-6. Highlights of the program will include a "Brief History of Blood Banking and Requirements," by Dr. Roderick Murray, chief, Biological Control Laboratories, National Institutes of Health, Bethesda, Md.; "Antigens and Antibodies of ABO Systems," Lt. Col. Joseph H. Akeroyd, Ph.D., assistant chief, Hematology Research Laboratory, Army Medical Center Grade School, Walter Reed Army Hospital, Washington, D. C.; "The Rh and HR Systems," Dr. William D. Dolan, department of pathology, Arlington Hospital, Arlington, Va., and instructor in pathology, Georgetown University School of Medicine, Washington, D. C.; "Problems and Hazards in Transfusing," Dr. Oscar B. Hunter Jr., director, Hunter Memorial Laboratory, and instructor in clinical medicine, Georgetown University School of Medicine, Washington, D. C.; "Transfusion in Disease, Blood Substitutes and Fractions," Dr. Sam T. Gibson, medical director, American National Red Cross, Washington, D. C.; and "Other Miscellaneous Blood Groups and Their Aspects in Blood Transfusions," Dr. Milton S. Sacks, professor of clinical medicine, and chief, division of clinical pathology, University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore.

Pathologists Meet in St. Louis.—On April 7 and 8 at St. Louis University School of Medicine, 1402 S. Grand Ave., St. Louis, the Missouri Society of Pathologists and the Kansas Society of Pathologists will sponsor a South Central Regional Meeting of the College of American Pathologists (in cooperation with the Federal Civil Defense Administration, the Public Health Service, and the Armed Forces) on "The Role of Medical Laboratories in Defense and Disaster." The Monday program will include: "General Aspects of Civil Defense with Particular Emphasis on the Health-Medical Role of the Federal Civil Defense Administration," by Dr. Paul A. Lindquist, regional medical director of the Federal Civil Defense Administration, who will later give a summary and outline the needs for further study and discussion. Among the topics to be discussed will be "The Role of the Pathologist in the Initial Phase of a Catastrophe," "The Integration of Private and Hospital Laboratories with Public Health Laboratories in a Disaster Area," "The Integration of Civilian Laboratories with the Armed Forces Laboratories in a Disaster Area," "Bacteriological and Biological Warfare," "Survival Pattern Following Radiation Bombing," "Hematological Findings in Radiation Catastrophe," and "Fluid, Electrolyte and Blood Replacements in Radiation Casualties." On Sunday the presentation of papers on "The Role of Blood Banks in Disaster Programs," "The Clearing House Program of the American Association of Blood Banks," and "The Needs for a State Blood Bank Organization" will precede the organizational meeting of the Missouri Blood Bank Association. The meetings will be open to all interested physicians, medical technologists, hospital administrators, and other medical and hospital personnel. For information, write Dr. Henry C. Allen, Secretary, Missouri Society of Pathologists, 35 N. Central Ave., Clayton 5, Mo.

Society News.—Dr. W. Alan Wright, medical director, Pfizer Laboratories, Brooklyn, N. Y., was recently elected president of the **Association of Medical Directors;** Dr. John B. Jewell, Ayerst Laboratories, New York, vice-president; and Dr. Ben Lanman, Schenley Laboratories, New York, secretary.——Newly elected officers of the **American College of Radiology** include Dr. Wilbur

Bailey, Los Angeles, president, and Dr. James P. Rousseau, Winston-Salem, N. C., vice-president.——The **Western Society for Clinical Research** recently elected Dr. William M. Kirby, Seattle, president; Dr. Gordon Meiklejohn, Denver, vice-president; and Dr. Arthur J. Seaman, Portland, secretary-treasurer. ——Officers of the **American Academy of Allergy** include Dr. Carl E. Arbesman, Buffalo, president; Dr. William B. Sherman, New York, president-elect; Dr. William P. Buffum, Providence, R. I., vice-president; Dr. Francis C. Lowell, Boston, secretary; and Dr. Max Samter, Oak Park, Ill., treasurer.——Officers of the **American Society for Surgery of the Hand** include Dr. Lot D. Howard Jr., San Francisco, president; Dr. J. Edward Flynn, Boston, president-elect; Dr. Jerome P. Webster, New York, vice-president; and Dr. George S. Phalen, Cleveland, secretary-treasurer.——Newly elected officers of the **South Atlantic Association of Obstetricians and Gynecologists** include Dr. John C. Burwell Jr., Greensboro, N. C., president; Dr. George A. Williams, Atlanta, Ga., vice-president; Dr. Manly E. Hutchinson, Columbia, S. C., president-elect; Dr. C. Hampton Mauzy, Winston-Salem, N. C., secretary-treasurer; and Dr. W. Norman Thornton, Charlottesville, Va., assistant secretary-treasurer. The next meeting of the association will be held at the Francis Marion Hotel, Charleston, S. C., Feb. 6-9, 1957.——The **American Foundation for Allergic Diseases** (274 Madison Ave., New York 16) has announced plans for a $1,100,000 campaign to carry out a program of professional training, public education, and fundamental research. The major research areas selected include the following: (1) studies of the ways in which cells of the body are affected by "antigens"; (2) studies of ways to prevent antibody formation so that no reactions occur when sensitizing antibodies meet the "antigens" for which they are specific; (3) study of histamine metabolism; (4) further study of enzymes; (5) basic research into the causes of autosensitization; (6) advanced research in the collagen diseases; and (7) studies of psychophysiological factors in allergy. The foundation plans to offer postdoctoral research fellowships to qualified physicians and scientists. Research grants will be limited to three years but may be renewed at the end of that period. Each grant will carry with it a supplemental grant to be paid to the institution in which the work will be done. The number of fellowships will vary from year to year, depending on the quality of the applicants.——At its first meeting, Jan. 25, in Carmel, Calif., under the presidency of Dr. Robert H. Williams, professor of medicine, University of Washington School of Medicine, Seattle, the **Western Association of Physicians** chose the following officers for 1956-1957: Dr. Maxwell M. Wintrobe, professor of medicine, University of Utah School of Medicine, Salt Lake City, president; Dr. Theodore L. Althausen, professor of medicine, University of California School of Medicine, San Francisco, vice-president; Dr. Joseph F. Ross, associate dean and professor of medicine and radiobiology, University of California at Los Angeles School of Medicine, secretary-treasurer; and Drs. David A. Rytand, professor of medicine, Stanford University School of Medicine, San Francisco, Clement A. Finch, professor of medicine, University of Washington School of Medicine, Seattle, John S. Lawrence, professor of medicine, University of California at Los Angeles School of Medicine, and Gordon Meiklejohn, professor of medicine, University of Colorado School of Medicine, Denver, councilors. The objective of the association is to provide meetings for persons with an established, active role in clinical research. Experimentation will be conducted with different types of scientific reports. Many of the essayists will present not only their recent investigations but also summaries of progress in their respective fields. The scientific programs for the Western Association of Physicians, for the Western Society for Clinical Research, and for the western section of the American Federation for Clinical Research are to be integrated.——The meeting of the eastern section of the **American Congress of Physical Medicine and Rehabilitation** will be held at the Hotel Adelphia in Philadelphia April 7. Inquiries may be addressed to secretary of the section, Dr. Harold Lefkoe, 1006 Medical Tower, 255 S. 17th St., Philadelphia 3.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1956 Annual Meeting, Chicago, June 11-15.
1956 Clinical Meeting, Seattle, Nov. 27-30.
1957 Annual Meeting, New York, June 3-7.
1957 Clinical Meeting, Philadelphia, Dec. 3-6.
1958 Annual Meeting, San Francisco, June 23-27.
1958 Clinical Meeting, Minneapolis, Dec. 2-5.

AERO MEDICAL ASSOCIATION, Drake Hotel, Chicago, Apr. 16-18. Dr. Thomas H. Sutherland, P. O. Box 26, Marion, Ohio, Secretary.

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Birmingham, Apr. 19-21. Dr. Douglas L. Cannon, 537 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF NEUROLOGY, Hotel Jefferson, St. Louis, Apr. 23-28. Dr. Thomas W. Farmer, Dept. of Medicine, University of North Carolina, Chapel Hill, N. C., Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Rice Hotel and Sam Houston Coliseum, Houston, Texas, Apr. 16-19. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Illinois, Executive Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Milwaukee, Apr. 4-6. Dr. Normand L. Hoerr, 2109 Adelbert Rd., Cleveland 6, Secretary.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION, Muehlebach Hotel, Kansas City, Mo., May 3-5. Dr. Richard C. Webster, 1101 Beacon Street, Brookline 46, Mass., Chairman, Program Committee.

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE, Washington Duke Hotel, Durham, N. C., Apr. 19-21. Dr. Ilza Veith, 950 East 59th St., Chicago 37, Executive Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, Chalfonte-Haddon Hall, Atlantic City, N. J., Apr. 16-20. Dr. F. S. Cheever, Univ. of Pittsburgh, School of Public Health, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, Netherland Plaza Hotel, Cincinnati, Apr. 26-28. Dr. Edward A. Gall, Dept. of Pathology, Cincinnati General Hospital, Cincinnati 29, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, Apr. 10-12. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Fontainebleau Hotel, Miami Beach, Fla., May 7-9. Dr. Paul C. Samson, 3959 Happy Valley Road, Lafayette, Calif., Secretary.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION, Sheraton-Mt. Royal Hotel, Montreal, Canada, May 15-16. Dr. F. Johnson Putney, 1719 Rittenhouse Square, Philadelphia 3, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, Hotel New Yorker, New York, Apr. 15-20. Dr. Fred W. Wittich, 401 Marquette Bank Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF CARDIOLOGY, Drake Hotel, Chicago, May 16-18. Dr. Philip Reichert, Empire State Bldg., New York 1, Secretary.

AMERICAN COLLEGE HEALTH ASSOCIATION, Hotel Nicollet, Minneapolis, May 17-19. Dr. Irvin W. Sander, Wayne University, Detroit, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Biltmore Hotel and Shrine Auditorium, Los Angeles, Apr. 16-20. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Chalfonte-Haddon Hall, Atlantic City, N. J., April 29. Dr. William W. Stead, VA Hospital, Minneapolis 17, Secretary.

AMERICAN GASTROENTEROLOGICAL ASSOCIATION, Claridge Hotel, Atlantic City, N. J., Apr. 27-28. Dr. H. Marvin Pollard, University Hospital, Ann Arbor, Mich., Secretary.

AMERICAN GERIATRICS SOCIETY, Palmer House, Chicago, May 3-4. Dr. Malford W. Thewlis, 25 Mechanic St., Wakefield, R. I., Secretary.

AMERICAN GOITER ASSOCIATION, Drake Hotel, Chicago, May 3-5. Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., Secretary.

AMERICAN GYNECOLOGICAL SOCIETY, The Shoreham, Washington, D. C., May 21-23. Dr. John I. Brewer, 104 South Michigan Ave., Chicago 3, Secretary.

AMERICAN INDUSTRIAL HYGIENE ASSOCIATION, Convention Hall, Philadelphia, April 23-27. Dr. Henry F. Smyth Jr., Mellon Institute, Fifth Ave., Pittsburgh 13, Executive Secretary.

AMERICAN LARYNGOLOGICAL ASSOCIATION, Seigniory Club, Canada, May 13-14. Dr. Harry P. Schenck, 326 South 19th St., Philadelphia 3, Secretary.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Sheraton-Mt. Royal Hotel, Montreal, Canada, May 15-17. Dr. Steward Nash, 277 Alexander St., Rochester 7, N. Y., Secretary.

AMERICAN OTOLOGICAL SOCIETY, Seigniory Club, P.Q., Canada, May 11-12. Dr. Laurence R. Boies, 90 South Ninth St., Minneapolis 2, Secretary.

AMERICAN PEDIATRIC SOCIETY, The Inn, Buck Hill Falls, Pa., May 6-11. Dr. Alms C. McGuinness, Memorial Hospital Association of Kentucky, 1427 I St., N.W., Washington 5, D. C., Secretary.

AMERICAN PHYSIOLOGICAL SOCIETY, Atlantic City, N. J., Apr. 16-20. Dr. Allan C. Burton, University of Western Ontario, London, Ontario, Canada, Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Chicago, April 30-May 4. Dr. William Malamud, 80 East Concord St., Boston 18, Secretary.

AMERICAN RADIUM SOCIETY, Shamrock Hotel, Houston, Texas, Apr. 9-11. Dr. Robert E. Fricke, 102 Second Ave. S.W., Rochester, Minn., Secretary.

AMERICAN SOCIETY FOR ARTIFICIAL INTERNAL ORGANS, Atlantic City, N. J., Apr. 15-16. Dr. Peter F. Salisbury, Institute for Medical Research, 4751 Fountain Ave., Los Angeles 29, Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, Chalfonte-Haddon Hall, Atlantic City, N. J., Apr. 15-19. Dr. Philip Handler, Duke University, Durham, N. C., Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Chalfonte-Haddon Hall, Atlantic City, N. J., April 30. Dr. J. D. Myers, University of Pittsburgh School of Medicine, Pittsburgh 13, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, Atlantic City, N. J., Apr. 15-21. Dr. Cyrus C. Erickson, 874 Union Ave., Memphis 3, Tenn., Secretary.

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Atlantic City, N. J., Apr. 15-20. Dr. Carl C. Pfeiffer, Emory University School of Medicine, Emory University, Ga., Secretary.

AMERICAN SURGICAL ASSOCIATION, The Greenbrier, White Sulphur Springs, W. Va., Apr. 11-13. Dr. R. Kennedy Gilchrist, 59 East Madison St., Chicago 3, Secretary.

AMERICAN TRUDEAU SOCIETY, Hotel Statler, New York, May 21-25. Mr. Frank W. Webster, 1790 Broadway, New York 19, Executive Secretary.

ARIZONA MEDICAL ASSOCIATION, San Marcos Hotel, Chandler, Apr. 25-28. Dr. D. W. Melick, 411 Security Bldg., Phoenix, Secretary.

ARKANSAS MEDICAL SOCIETY, Hotel Marion and Robinson Auditorium, Little Rock, Apr. 23-25. Mr. Paul C. Schaefer, 213 Kelley Bldg., Ft. Smith, Executive Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Chalfonte-Haddon Hall, Atlantic City, N. J., May 1-2. Dr. Paul B. Beeson, Yale University School of Medicine, New Haven 11, Conn., Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS AND SURGEONS, Columbus, Ohio, Apr. 5-7. Dr. William L. Baughn, 1635 West 25th St., Anderson, Ind., Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Ambassador Hotel, Los Angeles, April 29-May 2. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

CONNECTICUT STATE MEDICAL SOCIETY, Hamden, Apr. 24-26. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Executive Secretary.

EASTERN SECTION, AMERICAN CONGRESS OF PHYSICAL MEDICINE AND REHABILITATION, Hotel Adelphia, Philadelphia, April 7. Dr. Harold Lefkoe, 1006 Medical Tower, Philadelphia 3, Secretary.

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, Chalfonte-Haddon Hall, Atlantic City, N. J., Apr. 16-20. Mr. M. O. Lee, 2101 Constitution Ave., Washington 25, D. C., Secretary.

FLORIDA MEDICAL ASSOCIATION, Hotel Fontainebleau, Miami Beach, May 13-16. Dr. Samuel M. Day, P.O. Box 1018, Jacksonville, Secretary.

GEORGIA, MEDICAL ASSOCIATION OF, Atlanta-Biltmore Hotel, Atlanta, May 13-16. Dr. David Henry Poer, 875 W. Peachtree St., Atlanta, Secretary.

HAWAII MEDICAL ASSOCIATION, Reef Hotel, Honolulu, Apr. 22-29. Dr. William S. Ito, 510 S. Beretania St., Honolulu, Secretary.

ILLINOIS STATE MEDICAL SOCIETY, Hotel Sherman, Chicago, May 15-18. Dr. Harold M. Camp, 224 S. Main St., Monmouth, Secretary.

INDUSTRIAL MEDICAL ASSOCIATION, Philadelphia, Apr. 23-26. Dr. H. Glenn Gardiner, Inland Steel Co., East Chicago, Ind., Secretary.

INTERNATIONAL ACADEMY OF PROCTOLOGY, Drake Hotel, Chicago, Apr. 23-26. Dr. Alfred J. Cantor, 43-55 Kissena Blvd., Flushing, N. Y., Secretary.

INTERSTATE ORTHOPEDIC SOCIETY, Pittsburgh, April 18. Dr. Harold H. Sankey, 121 University Place, Pittsburgh 13, Secretary.

IOWA STATE MEDICAL SOCIETY, Savery Hotel and Veterans Memorial Auditorium, Des Moines, Apr. 22-25. Mr. Donald L. Taylor, 529 36th St., Des Moines 12, Executive Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Alabama, Apr. 8-13. Dr. Eugene H. Dibble Jr., John A. Andrew Memorial Hospital, Tuskegee Institute, Ala., Secretary.

KANSAS MEDICAL SOCIETY, Jayhawk Hotel, Topeka, April 29-May 3. Mr. Oliver E. Ebel, 315 West 4th St., Topeka, Executive Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Hotel Bentley, Alexandria, Apr. 23-25. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, BALTIMORE, May 2-4. Dr. Everett S. Diggs, 1211 Cathedral St., Baltimore 1, Secretary.

MASSACHUSETTS MEDICAL SOCIETY, Hotel Statler, Boston, May 22-24. Dr. Robert W. Buck, 22 The Fenway, Boston 15, Secretary.

MICROCIRCULATORY CONFERENCE, Hotel Schroeder, Milwaukee, Apr. 3. Dr. George P. Fulton, Boston University, College of Liberal Arts, 725 Commonwealth Ave., Boston 15, Chairman.

MINNESOTA STATE MEDICAL ASSOCIATION, Hotel Kahler, Rochester, May 21-23. Mr. R. R. Rosell, 496 Lowry Medical Arts Bldg., St. Paul 2, Executive Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Hotel Heidelberg, Jackson, May 8-10. Mr. Rowland B. Kennedy, 860 Milner Bldg., Jackson, Executive Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, Apr. 8-11. Dr. E. Royse Bohrer, 634 North Grand Blvd., St. Louis 3, Secretary.

NATIONAL TUBERCULOSIS ASSOCIATION, Hotel Statler, New York, May 21-25. Dr. James E. Perkins, 1790 Broadway, New York 19, Managing Director.

NEBRASKA STATE MEDICAL ASSOCIATION, Hotel Cornhusker, Lincoln, May 14-17. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln 8, Secretary.

NEW ENGLAND HEALTH EDUCATION ASSOCIATION, University of Connecticut, Storrs, Conn., May 11-12. Miss Wyntha Tompkins, Middlesex Health Association, Essex, Mass., Secretary.

NEW JERSEY, MEDICAL SOCIETY OF, Haddon Hall, Atlantic City, May 13-16. Dr. Marcus H. Greifinger, 315 West State St., Trenton 8, Secretary.

NEW MEXICO MEDICAL SOCIETY, Roswell Senior High School, Roswell, May 2-4. Mr. Ralph R. Marshall, 221 West Central Ave., Albuquerque, Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, New York, May 7-11. Dr. Walter P. Anderton, 386 Fourth Ave., New York 16, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, April 30-May 2. Dr. Millard D. Hill, 203 Capitol Bldg., Raleigh, Secretary.

OGDEN SURGICAL SOCIETY, Ogden Theater, Ogden, Utah, May 23-25. Dr. Wendell J. Thomson, 2404 Washington Ave., Ogden, Utah, President.

OHIO STATE MEDICAL ASSOCIATION, Cleveland, Apr. 10-13. Mr. Charles S. Nelson, 79 East State St., Columbus 15, Executive Secretary.

OHIO STATE RADIOLOGICAL SOCIETY, Deshler-Hilton Hotel, Columbus, May 11-13. Dr. John R. Hannan, 10515 Carnegie Ave., Cleveland 6, Secretary.

OKLAHOMA STATE MEDICAL ASSOCIATION, Municipal Auditorium, Oklahoma City, May 6-9. Mr. R. H. Graham, 1227 Classen Drive, Oklahoma City, Executive Secretary.

REGIONAL MEETINGS:

AMERICAN COLLEGE OF GASTROENTEROLOGY:

New Orleans, Auditorium, Louisiana State University, April 8. Mr. Daniel Weiss, 33 West 60th St., New York 23, Executive Secretary.

AMERICAN COLLEGE OF SURGEONS:

Edmonton, Alberta, Canada, The Macdonald, Apr. 23-25. Dr. J. Rose Vant, 10113, 104th St., Edmonton, Alberta, Canada, Chairman.

U. S. SECTION, INTERNATIONAL COLLEGE OF SURGEONS:

Madison, Wis., Loraine Hotel, April 26-28. Dr. Arnold S. Jackson, Jackson Clinic, Madison, Wis., Chairman.

Chattanooga, Tenn., Read House, April 30-May 1. Dr. William G. Stephenson, 546 McCallie Ave., Chattanooga 3, Tenn., Chairman.

RHODE ISLAND MEDICAL SOCIETY, Rhode Island Medical Society Library, Providence, May 1-3. Dr. Thomas Perry Jr., 106 Francis St., Providence 3, Secretary.

SOCIETY OF BIOLOGICAL PSYCHIATRY, Morrison Hotel, Chicago, Apr. 28-29. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 5, Secretary.

SOCIETY OF NEUROLOGICAL SURGEONS, Memphis, Tenn., May 7-8. Dr. Bronson S. Ray, 525 East 68th St., New York 21, Secretary.

SOCIETY FOR PEDIATRIC RESEARCH, The Inn, Buck Hill Falls, Pa., May 6-11. Dr. Sydney S. Gellis, 330 Brookline Ave., Boston 15, Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Ocean Forest Hotel, Myrtle Beach, May 15-17. Dr. Robert Wilson, 165 Rutledge Ave., Charleston, Secretary.

SOUTHERN OREGON MEDICAL SOCIETY, Klamath Falls, May 9. Dr. Calvin Hunt, 1842 Esplanade St., Klamath Falls, Secretary.

SOUTHWESTERN SURGICAL CONGRESS, Pioneer Hotel, Tucson, Ariz., Apr. 16-18. Dr. C. M. O'Leary, 207 Plaza Court Bldg., Oklahoma City, Secretary.

STUDENT AMERICAN MEDICAL ASSOCIATION, Hotel Sherman, Chicago, May 4-6. Mr. Russell F. Staudacher, 510 North Dearborn St., Chicago 10, Executive Secretary.

SYMPOSIUM ON PEDIATRICS, Salt Lake City, Apr. 12-13. Dr. F. Willis Taylor, 1265 West 4th North, Salt Lake City 16, Chairman.

TENNESSEE STATE MEDICAL ASSOCIATION, Peabody Hotel, Memphis, Apr. 8-11. Dr. R. H. Kampmeier, 112 Louise Ave., Nashville 5, Secretary.

TEXAS MEDICAL ASSOCIATION, Galveston, Apr. 21-25. Mr. C. Lincoln Williston, 1801 N. Lamar Blvd., Austin, Executive Secretary.

THE CONSTANTINIAN SOCIETY, Del Monte Lodge, Pebble Beach, Calif., Apr. 11-14. Dr. C. F. Shook, P. O. Box 1035-36, Toledo 1, Ohio, Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Mexicali, Baja Calif., and Calexico, Calif., Apr. 13-16. Dr. Sidney B. Clark, 204 U. S. Court House, El Paso, Texas, Secretary.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION, Hotel Ambassador, Los Angeles, Apr. 28. Dr. Edward J. Zaik, 740 S. Olive St., Room 220, Los Angeles 14, Secretary.

WESTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Sheraton-Palace Hotel, San Francisco, April 30-May 3. Dr. James Ownby Jr., 516 Sutter St., San Francisco, Chairman.

WISCONSIN, STATE MEDICAL SOCIETY OF, Hotel Schroeder, Milwaukee, May 1-3. Mr. Charles H. Crownhart, 330 East Lakeside St., Madison 1, Secretary.

FOREIGN AND INTERNATIONAL

ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS, London School of Hygiene and Tropical Medicine, London W.C.1, England, Sept. 24-28, 1956. Dr. J. A. A. Mekelburg, Peek, Frean and Company, Ltd., Keetons Rd., Bermondsey, London, S.E.16, England, Honorable Secretary.

BRITISH MEDICAL ASSOCIATION, Brighton, England, July 9-13, 1956. Dr. Angus Macrae, B. M. A. House, Tavistock Square, London, W.C.1, England.

CANADIAN MEDICAL ASSOCIATION, Quebec, P. Q., Canada, June 10-14, 1956. Dr. Arthur D. Kelly, 150 St. George St., Toronto 5, Ont., Canada, Secretary.

CONFERENCE OF INTERNATIONAL UNION FOR HEALTH EDUCATION OF THE PUBLIC, Rome, Italy, April 27-May 5, 1956. Mr. Lucien Viborel, 92 rue St. Denis, Paris 1er, France, Secretary-General.

CONGRESS OF FRENCH SOCIETY OF OPHTHALMOLOGY, Paris, France, May 6-10, 1956. Dr. Marcel Kalt, 81 rue Saint-Lazare, Paris 9e, France, Secretary.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Miami Beach, Fla., U.S.A., April 9-12, 1956. For information write: Mrs. L. McMechan, 318 Hotel West Lake, Rocky River, Ohio, U. S. A.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LIMNOLOGY, Helsinki, Finland, July 26-Aug. 7, 1956. For information address: Dr. H. Luther, Snellmansgatan 16 C 36, Helsinki, Finland.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LOGOPEDICS AND PHONIATRICS, Barcelona, Spain, Sept. 3-7, 1956. Dr. J. Perello, Provenza 319, Barcelona 9, Spain, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF HEMATOLOGY, Hotel Somerset, Boston, Mass., U.S.A., Aug. 27-Sept. 1, 1956. Dr. W. C. Moloney, 39 Bay State Road, Boston, Mass., U.S.A., Secretary.

CONGRESS OF INTERNATIONAL UNION AGAINST TUBERCULOSIS, New Delhi, India, Jan. 3-6, 1957. For information address: Secretariat, The Union, 66 Boulevard Saint-Michel, Paris 6e, France.

CONGRESS OF LATIN SOCIETY OF OPHTHALMOLOGY, Madrid, Spain, April 24-28, 1956. For information address: Dr. Costi, Montalban 3, Madrid, Spain.

EUROPEAN CONGRESS OF ALLERGOLOGY, Florence, Italy, Sept. 12-15, 1956. Prof. Umberto Serafini, Instituto de Patologia Medica, Viale Morgagni, Florence, Italy, Secretary-General.

EUROPEAN CONGRESS OF CARDIOLOGY, Stockholm, Sweden, Sept. 10-14, 1956. Dr. Karl Erik Grewin, Sodersjukhuset, Stockholm, Sweden, General Secretary.

EUROPEAN SYMPOSIUM ON VITAMIN B_{12}, Hamburg, Germany, May 22-26, 1956. For information write: Doz. Dr. H. Bauer, Nervenklinik, Hamburg-Eppendorf, Germany.

HEALTH CONGRESS, ROYAL SOCIETY FOR THE PROMOTION OF HEALTH, Blackpool, England, April 24-27, 1956. Mr. P. Arthur Wells, 90 Buckingham Palace Road, London S.W. 1, England, Secretary.

INTER-AMERICAN CONGRESS OF CARDIOLOGY, Havana, Cuba, Nov. 4-10, 1956. For information address: Dr. Ramon Aixala, Apartado 2108, Havana, Cuba.

INTERNATIONAL ACADEMY OF PATHOLOGY, Cincinnati, Ohio, U. S. A., April 24-25, 1956. Dr. F. K. Mostofi, Armed Forces Institute of Pathology, Washington 25, D. C., U. S. A., Secretary.

INTERNATIONAL CONGRESS AGAINST ALCOHOLISM, Istanbul, Turkey, Sept. 10-15, 1956. For information address: International contre l'Alcoolisme, Case Gare 49, Lausanne, Switzerland.

INTERNATIONAL CONGRESS ON ANIMAL REPRODUCTION, Arts School, University of Cambridge, Cambridge, England, June 25-30, 1956. Dr. Joseph Edwards, Production Division, Milk Marketing Board, Thames Ditton, Surrey, England, Hon. Secretary.

INTERNATIONAL CONGRESS OF ANTHROPOLOGICAL AND ETHNOLOGICAL SCIENCES, Philadelphia, Pa., U. S. A., Sept. 2-9, 1956. Dr. William N. Fenton, National Research Council, Division of Anthropology and Psychology, 2101 Constitution Avenue, Washington 25, D. C., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF DIETETICS, Congress Palace, Esposizione Universale Roma, Rome, Italy, Sept. 10-14, 1956. Prof. E. Serianni, Associazione Dietetica, Italiana, via dei Penitenzieri N. 13, Rome, Italy, Secretary General.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Cologne, Germany, Aug. 19-23, 1956. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, U. S. A., Executive Director.

INTERNATIONAL CONGRESS OF ENTOMOLOGY, Montreal, Canada, Aug. 17-25, 1956. Mr. J. A. Downes, Science Service Bldg., Carling Ave., Ottawa, Ont., Canada, Secretary.

INTERNATIONAL CONGRESS OF GASTROENTEROLOGY, London, England, July 18-21, 1956. Mr. Hermon Taylor, London Hospital, White Chapel, London E.1, England, Honorable Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Maison de la Mutualite, Paris, France, June 5-8, 1956. For information address: Mr. M. H. Thoillier, 37 Rue de Monthlon, Paris 9e, France.

INTERNATIONAL CONGRESS FOR THE HISTORY OF SCIENCE, Florence and Milan, Italy, Sept. 3-10, 1956. Dr. M. L. Bonelli, Instituto di Ottica, Arcetri, Florence, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF HUMAN GENETICS, Copenhagen, Denmark, Aug. 1-6, 1956. For information address: The University Institute for Human Genetics, Tagensvej 14, Copenhagen N, Denmark.

INTERNATIONAL CONGRESS OF HYDATID DISEASE, Athens, Greece, Sept. 14-18, 1956. Prof. B. Kourias, Croix-Rouge Hellenique, 1 rue Mackenzie King, Athens, Greece, Secretary-General.

INTERNATIONAL CONGRESS ON INFECTIOUS PATHOLOGY, Lyon, France, May 24-26, 1956. General Secretariat: Institut Pasteur de Lyon, 77 rue Pasteur, Lyon, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Madrid, Spain, Sept. 19-23, 1956. Dr. J. C. De Oya and Dr. J. Gimena, Hostaleza No. 90, Madrid, Spain, Secretaries.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Palmer House, Chicago, Illinois, U. S. A., Sept. 9-13, 1956. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF MEDICAL RADIOPHOTOGRAPHY, Paris, France, April 4-7, 1956. For information address: Secretariat, 66 Boulevard Saint Michel, Paris 6e, France.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, Shoreham Hotel, Washington, D. C., U. S. A., Oct. 1-5, 1956. For information address: Miss Doris Gleason, Executive Director, American Association of Medical Record Librarians, 510 North Dearborn St., Chicago 10, Illinois, U. S. A.

INTERNATIONAL CONGRESS OF NEO-HIPPOCRATIC MEDICINE, Montecatini, Terme, Italy, May 20-22, 1956. Dr. Valente, 41 Avenue Verdi, Montecatini Terme, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Copenhagen, Denmark, July 22-27, 1956. Professor P. Plum, Rigshospitalet, Copenhagen, Denmark, President.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, Copenhagen, Denmark, August 20-24, 1956. Dr. B. Strandberg, Kobenhavns amts sygehus i Gentofte, Dept. of Rheumatology and Physical Medicine, Hellerup, Denmark, Honorable Secretary.

INTERNATIONAL CONGRESS OF RADIOLOGY, Mexico, D. F., Mexico, July 22-28, 1956. Dr. Jose Noriega, Tepic 126 (2e piso), Mexico, D. F. 7, Mexico, Secretary General.

INTERNATIONAL CONGRESS OF WORLD CONFEDERATION FOR PHYSICAL THERAPY, Hotel Statler, New York, New York, U. S. A., June 17-23, 1956. For information address: Miss Mildred Elson, American Physical Therapy Association, 1790 Broadway, New York 19, New York, U. S. A.

INTERNATIONAL GENETICS SYMPOSIUM, Tokyo and Kyoto, Japan, Sept. 6-12, 1956. For information address: Secretary, International Genetics Symposium, Science Council of Japan, Ueno Park, Tokyo, Japan.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Brussels, Belgium, July 29-Aug. 5, 1956. For information address: Prof. J. Reuse, Faculte de Medicine et de Pharmacie, 115 Boulevard de Waterloo, Brussels, Belgium.

INTERNATIONAL PROFESSIONAL UNION OF GYNECOLOGISTS AND OBSTETRICIANS, Madrid, Spain, Sept. 28-29, 1956. Dr. Jacques Courtois, 1 rue Racine, St-Germain-en-Laye (S and O), France, Permanent International Secretary-General.

INTERNATIONAL SYMPOSIUM ON DIENCEFALON, Musec della Scienza e della Tecnica, Piazza S. Vittorre 21, Milan, Italy, May 3-5, 1956. Drs. S. Curri and L. Martini, Instituto di Farmacologia, Universita di Milano, via Andre del Sarto 21, Milan, Italy, Secretaries.

INTERNATIONAL SYMPOSIUM ON VENEREAL DISEASES AND THE TREPONEMATOSES, Hotel Statler, Washington, D. C., U. S. A., May 28-June 1, 1956. For information address: Dr. Charles A. Smith, Chief, Venereal Disease Program, Division of Special Health Services, Public Health Service, Dept. of Health, Education and Welfare, Washington 25, D. C., U. S. A.

LATIN AMERICAN CHAPTER, INTERNATIONAL SOCIETY OF ANGIOLOGY, Havana, Cuba, Nov. 8-11, 1956. Dr. Armando Nuñez Nuñez, 25 No. 510 Vedado, Havana, Cuba, President.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, EXTRAORDINARY GENERAL ASSEMBLY, Burgenstock, Nidwalden, Switzerland, Sept. 21-24, 1956. Dr. Janet Aitken, 30a Acacia Road, London N.W. 1, England, Secretary.

MIDDLE EAST MEDICAL ASSEMBLY, Campus, American University of Beirut, Beirut, Lebanon, April 7-9, 1956. Dr. Virgil C. Scott, American University of Beirut, Beirut, Lebanon, Chairman.

NATIONAL CONGRESS OF PEDIATRICS, Cuidad Universitaria, Mexico D.F., Mexico, May 1-5, 1956. Dr. Ignacio Avila Cisneros, Calzada de Madereros No. 240, Mexico 18, D.F., Mexico, Coordinator.

NORTH QUEENSLAND MEDICAL CONFERENCE, Cairns, North Queensland, Australia, June 25-30, 1956. Dr. W. R. Horsfall, P.O Box 672, Cairns, N.Q., Australia, Secretary.

PAKISTAN MEDICAL CONFERENCE, University of Peshawar, Peshawar, Pakistan, Apr. 2-4, 1956. Dr. M. W. Alivi, 9, Braganza House, Napier St., Saddar, Karachi, Pakistan, Secretary General.

PAN AMERICAN CONGRESS ON CANCER CYTOLOGY, Miami, Fla., U. S. A., April 2-6, 1957. Dr. J. Ernest Ayre, 1155 N.W. 14th St., Miami, Fla. U. S. A., General Chairman.

PAN AMERICAN CONGRESS OF GERONTOLOGY, Mexico, D. F., Mexico, Sept. 7-15, 1956. Dr. Manuel Payno, Avenue Cuahtemoc No. 10-3, Mexico 7, D. F., Mexico, Presidente.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, San Juan, Puerto Rico, April 8-12, 1956. Dr. C. E. Munoz MacCormick, Apartado 9111, Santurce 29, Puerto Rico, Secretary General.

PAN AMERICAN TUBERCULOSIS CONGRESS, Medellin and Bogota, Columbia, South America, Aug. 1-15, 1956. General Secretary, 26 de Marzo 1065, Montevideo, Uruguay.

WORLD CONGRESS ON FERTILITY AND STERILITY, Naples, Italy, May 18-24, 1956. Dr. Maxwell Roland, 114-20 Queens Boulevard, Forest Hills 75, New York, N. Y., U. S. A., Chairman, Liaison Committee.

WORLD FEDERATION FOR MENTAL HEALTH, Munich, Germany, Aug. 12-18, 1956. Secretariat, 19 Manchester Street, London W.1, England.

WORLD MEDICAL ASSOCIATION, Havana, Cuba, Oct. 9-15, 1956. Dr. Louis H. Bauer, 345 East 46th St., New York 17, New York, U. S. A., Secretary-General.

EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations in the United States and Canada, July 20. Final date for filing application was Jan. 20. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15, Conn.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY. *Written.* Various centers, July 26. *Oral.* St. Louis, Oct. 12-15. Final date for filing applications is April 1. Sec., Dr. B. M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 15, 1956. Final date for filing application is May 1. *Oral Examinations in 1956.* Los Angeles, April 12-14; Chicago, June 7-9. Final date for filing application for these three oral examinations was Jan. 3. New York City, Sept. 21-25. Final date for filing application is April 1. *Cardiovascular Disease.* Chicago, June 6. The number of candidates is limited to 24 and the final date for filing applications is Apr. 2. Exec. Sec., Dr. William A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: St. Louis, May 3-5. Sec., Dr. Leonard T. Furlow, 660 South Kingshighway, St. Louis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Oral and Pathological Examinations. Part II.* Chicago, May 11-20, 1956. *Part I.* Applications now being accepted. Final date for filing applications is Oct. 1. Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical Examination.* San Francisco, June 18-21, St. Louis, Oct. 20-24. *Written.* Jan. 21, 1957. Applications must be filed before July 1, 1956. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I. Oral and written.* Various centers, April, 1956. Final date for filing application was Nov. 30. *Oral. Part II.* Chicago, January 1957. Final date for filing application is Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY. *Oral.* Montreal, Canada, May 6-10. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: *Pathologic Anatomy and Clinical Pathology.* Boston, April 18-20. Final date for filing application was March 15. Sec., Dr. Edward B. Smith, 1040 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral, Part II.* Atlantic City, May 3-5; Cincinnati, June 8-10; New York City, Oct. 12-14, and San Francisco, Dec. 7-9. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION. *Parts I and II.* Chicago, June 16-17. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY. *Entire Examination.* Buffalo, May 13-15. Final date for filing case reports was Jan. 1. Corres. Sec., Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Oral and Written. Public Health.* Given at Columbia, California, Harvard, Tulane and Minnesota schools of public health. *Aviation Medicine.* Chicago, April 13-15. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY: *Part I.* Philadelphia, May 5. Final date for filing application was March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Philadelphia, April 16-18, 1956. Sec., Dr. David A. Boyd, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: Chicago, June 5-9. Final date for filing applications was Jan. 1.; Los Angeles, Sept. 30-Oct. 4. Final date for filing applications is June 1. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part II.* Boston, May 14-15 and Philadelphia, June 4-5. Sec., Dr. John B. Flick, 255 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: February 1957. Sec., Dr. William Niles Wishard, 1711 N. Capitol Ave., Indianapolis 7.

BOARD OF THORACIC SURGERY. *Written.* Various centers throughout the country, September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines and forthcoming network television programs on medical subjects is published each week only for the information of readers of THE JOURNAL. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles and programs reported.*

TELEVISION

Monday, April 9

NBC-TV, 11 a. m. - noon EST. "Medical and Health News with Howard Whitman," a segment of the "Home" program.

NBC-TV, 9 p. m. EST. "Medic" features a teleplay on cancer of the larynx titled "Don't Count the Stars."

MAGAZINES

Saturday Evening Post, March 24, 1956

"The Children of Medicine Mountain," by Steven M. Spencer
High in the New Hampshire hills is the Crotched Mountain Rehabilitation Center. In the first unit of a proposed "village for handicapped individuals" crippled children are taught to live with their afflictions.

Look, April 17, 1956

"The State of the Nation's Health," by Roland H. Berg
In a major feature covering 16 pages of pictures and text, Look's medical editor discusses socioeconomic factors affecting medical care in the United States and tells "how we stand on cancer, the heart, mental illness, t.b., polio, diabetes, allergy, ulcers, arthritis and the common cold." The article states, "We have been winning the battle against acute diseases, but losing the war against chronic killers."

Redbook, April, 1956

"The Fear Campaign Against the Polio Vaccine," by Flora Rheta Schreiber
The author analyzes the motives behind "the fear campaign against the polio vaccine," which she says is conducted by Polio Prevention, Inc., Morris A. Bealle, and other organizations and personalities.

"How to Sleep," by Alton L. Blakeslee
"Some main points about sleep and how to get the right amount of it." According to the article, "only your doctor can advise you whether you need the aid of any kind of sleeping pills."

Family Circle, April, 1956

"It's an Emergency," by Mortimer Weber, M.D., as told to S. L. Engelbardt
Ten first-aid tips for parents, ranging from what to do (and what not to do) when an object is swallowed to how to take care of an open laceration.

Reader's Digest, April, 1956

"The Truth About Autopsies," by Albert Q. Maisel
"Old wives' tales and timeworn horror stories have blinded millions of us to the simple truth about autopsies." Actually, the author points out, postmortem studies have advanced scientific knowledge and often provide information of great help to the survivors.

"The One Sure Way to Reduce," by Blake Clark
"Combating overweight by diet alone is fighting with one hand behind our back." Dr. Jean Mayer of the department of nutrition of the Harvard School of Public Health says that "exercise is the other fist that would enable us to deal the knockout blow."

"The Uphill Fight Against Alcoholism," by Quentin Reynolds
Medical, religious, and communal organizations in Boston are striving to cope with the problem of alcoholism.

"The Rescue Squads Roll On," by James J. Kilpatrick and Charles Henry Hamilton
Some 850 rescue and first-aid units, manned by 26,000 volunteers, are in operation. Each is trained and equipped for any emergency endangering human life.

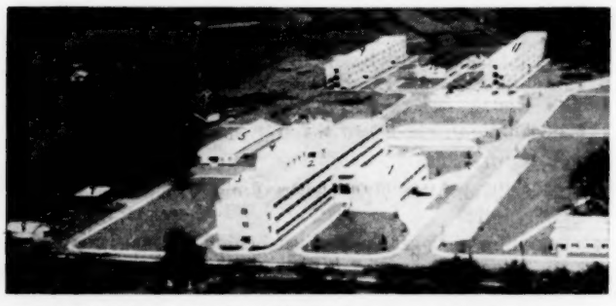
GOVERNMENT SERVICES

ARMY

Laboratory and Research Center in Japan.—The U. S. Army's principal medical laboratory and research center in the Far East, the 406th Medical General Laboratory, previously in Tokyo, moved with its assigned units to new buildings in the medical area at Camp Zama, Japan, on Feb. 15. Involved in the move were about 300 persons, of whom more than half were Japanese. The laboratory will occupy a modern four-story structure at its new location. Attached units under the command of Col. Joe M. Blumberg, in addition to the 406th Medical General Laboratory, include the 48th Medical Detachment, known better as the United Nations Blood Bank, and the Army Medical Research Detachment.

At Zama, officers, enlisted men, and Army civilians will be billeted in quarters only a short distance from the laboratory building. Dormitory facilities will also be available for the Japanese employees.

The 406th Medical General Laboratory furnishes diagnostic services in bacteriology, chemistry, medical zoology, pathology, serology, veterinary and food analysis, virology, entomology, and medical illustration. In addition, the laboratory procures and supplies whole blood to medical units in the Far East Command, conducts medical research, and trains armed forces personnel in laboratory methods. Among major research activities are studies on Japanese "B" encephalitis, scrub typhus, diarrhea, and soil and food bacteriology. Supported research has included studies on dysentery, epidemic hemorrhagic fever, infectious hepatitis, wound infection, and nutrition.



The 406th Medical General Laboratory area near Zama, Japan. The numbered buildings are: (1) headquarters, (2) laboratory, (3) Japanese employees' service, (4) medical supply, (5) blood storage and shipping, (6) animal barn, (7) aviary, (8) incinerator, (9) female bachelor officers' quarters, (10) officers' club, and (11) male bachelor officers' quarters.

Buildings of the new laboratory area include a headquarters building attached to the laboratory, enlisted men's barracks, a blood storage and shipping building, building for medical supplies, an incinerator, an aviary, and an animal barn. There are about 130 rooms and 125,000 sq. ft. of floor space in the headquarters and laboratory buildings.

NAVY

New Correspondence Course on X-Ray Fundamentals.—A correspondence course is now ready for distribution to eligible regular and reserve officer and enlisted armed forces medical department personnel. This course will provide physicians, x-ray technicians, and watch-standing personnel with well-grounded information in the fundamental principles of x-ray physics and technique along with biological hazards involved.

Consisting of four objective question-type assignments, the course is evaluated at 12 promotion and nondisability retirement points. Applications for the course should be submitted on form NavPers 992 and forwarded via official channels to the Commanding Officer, U. S. Naval Medical School, Bethesda 14, Md. Naval reserve officers and enlisted personnel who have completed the Special Clinical Services (general) correspondence course will not receive additional credit for completion of this course.

Personal.—The advisory medical board of the Leonard Wood Memorial for the Eradication of Leprosy (American Leprosy Foundation) elected Dr. Howard T. Karsner as its chairman on Feb. 25. Dr. Karsner, medical research advisor to the surgeon general, has been identified with work of the memorial for nearly 20 years.—Capt. William M. Silliphant, M. C., director, Armed Forces Institute of Pathology, Washington, D. C., has been appointed to the board of editors of the *American Journal of Clinical Pathology*. Capt. Edward C. Kenny, M. C., relieved Rear Adm. H. Lamont Pugh on March 2 as commanding officer of the National Naval Medical Center, Bethesda, Md. Admiral Pugh, former surgeon general of the Navy, is now undergoing treatment at the naval hospital in Bethesda.

ATOMIC ENERGY COMMISSION

New Procedures for Stable Isotope Distribution.—Simplified procedures for the distribution of stable (nonradioactive) isotopes and rare earths produced by the U. S. Atomic Energy Commission were announced by chairman Lewis L. Strauss Feb. 15. Under the revised procedures, neither domestic nor foreign applicants will be required to file and obtain commission approval before purchasing the materials. Requests will be handled directly between the user and the AEC facility supplying the materials. Electromagnetically concentrated stable isotopes will be available for sale to domestic users and reports of experiments using the materials will not be required.

The export of deuterium or deuterium compounds to any country listed as a subgroup A (Soviet bloc) country in Section 371.3 of the comprehensive export schedule of the U. S. Department of Commerce is prohibited. Export of deuterium or deuterium compounds to any other country requires a special export license from the Department of Commerce. Prior approval of the AEC must be obtained for sale of any other stable isotope to a person in a Soviet bloc country. The commission will distribute only materials that are not available commercially, unless the requestor certifies that the commercial product does not meet purity or quantity specifications required for his research.

Stable isotopes currently available for distribution include deuterium helium-3, boron-10 and 11, oxygen-18, argon-38, and the electromagnetically concentrated isotopes of about 80 elements. The rare earths included in the distribution program are those in the lanthanide series: elements 58 to 71 inclusive.

Stable isotopes, except deuterium, are distributed by the Stable Isotopes Research and Production Division, Oak Ridge National Laboratory, Oak Ridge, Tenn. The commission's Savannah River plant will sell deuterium oxide (heavy water) in bulk to any domestic distributor. The minimum and maximum amounts that may be purchased are 200 and 400 lb. respectively. Inquiries should be sent to the Savannah River Operation Office, U. S. Atomic Energy Commission, Post Office Box A, Aiken, S. C. Rare earth elements are available from the commission's Ames Laboratory, Iowa State College, Ames, Iowa. Purchasers may resell deuterium oxide in the smaller quantities used for research and development.

DEPARTMENT OF DEFENSE

Course on Heart Disease for Military and Civilian Doctors.—Doctors throughout the United States have been invited to attend an Armed Forces Institute of Pathology postgraduate course on heart disease in Washington, D. C., May 14-17. The course, which is another service of the institute, is designed to acquaint clinicians as well as pathologists with advances in this field. The instructors will include authorities from various medical centers. The course will be open to a total of 425 civilian and armed services physicians. Civilian physicians who desire to attend may apply to the Director, Armed Forces Institute of Pathology, Washington 25, D. C. Doctors in the armed forces should apply through normal military channels.

DEATHS

Harris, L. Marshall ✠ Captain, U. S. Navy, Newport, R. I.; born in Mineola, Texas, Dec. 24, 1900; University of Arkansas School of Medicine, Little Rock, 1931; specialist certified by the American Board of Obstetrics and Gynecology; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; fellow of the American College of Surgeons; at one time associate in obstetrics and gynecology at the Northwestern University Medical School in Chicago; served on the staffs of the Columbia, Georgetown, and Providence hospitals in Washington, D. C., and the Spohn Hospital in Corpus Christi, Texas; appointed a lieutenant (j. g.) in the U. S. Navy medical corps in 1931; promoted to the grade of captain in 1945; served during World War II; for meritorious service with the Marines in the field was awarded the Bronze Star medal with combat V; awarded the commendation ribbon for outstanding service as regimental surgeon of the Ninth Marines, Fleet Marine Force; recipient of the Purple Heart for wounds received in action in November, 1943; in 1945 medical officer in charge of the V-12 program in the Bureau of Medicine and Surgery with the Navy Department in Washington; served as chief of obstetrics and gynecology at the Naval hospitals in Great Lakes, Ill., and Bethesda, Md.; chief of dependents' service at the Naval Hospital in Newport, where he died Nov. 11, aged 54, of coronary thrombosis.

Campbell, Eldridge Houston, Jr. ✠ Albany, N. Y.; born in Alderson, W. Va., Dec. 20, 1901; Johns Hopkins University School of Medicine, Baltimore, 1927; interned at Johns Hopkins Hospital in Baltimore, where he served a residency; professor of surgery and chairman of the department at Albany Medical College; specialist certified by the American Board of Surgery; chairman of the American Board of Neurological Surgery; member of the American Surgical Association, Society of Neurological Surgeons, Southern Surgical Association, Harvey Cushing Society, Society of University Surgeons, and the American Neurological Association; fellow of the American College of Surgeons; during World War II was chief surgeon of the 33rd General Hospital, and was neurological consultant for the Mediterranean theater; in the Korean conflict was civilian consultant in neurological surgery to the surgeon general of the Army; translated from the Latin with James Colton "The Surgery of Theodoric"; surgeon in chief and attending neurosurgeon at Albany Hospital, where he died Feb. 15, aged 54, of carcinoma of the stomach.

King, Edward Daniel ✠ North Hollywood, Calif.; born Sept. 20, 1888; University of Cincinnati College of Medicine, 1912; clinical professor of otolaryngology at College of Medicine Evangelists, Loma Linda and Los Angeles; formerly on the faculty of his alma mater; member of the American Society of Plastic and Reconstructive Surgery, American Academy of Ophthalmology and Otolaryngology, American Laryngological Association, and the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; past-president of the Cincinnati Academy of Medicine; past-president of the Cincinnati League for the Hard of Hearing; at one time on the staffs of the Good Samaritan, Cincinnati General, and Children's hospitals in Cincinnati; served on the staffs of St. Joseph's Hospital in Burbank and the Presbyterian Hospital–Olmsted Memorial and Los Angeles County hospitals in Los Angeles; died Jan. 15, aged 67, of carcinoma of the pancreas.

Haynes, Royal Storrs, New York City; born in Dedham, Mass., Oct. 25, 1877; Columbia University College of Physicians and Surgeons, New York City, 1903; an associate member of the American Medical Association; member of the American Pediatric Society; at one time on the faculty of his alma mater; formerly recording secretary and trustee of the New York Academy of Medicine; served as director of the Junior Red Cross in Europe during World War I; helped create L'École de Puériculture in Paris and the Argonne Association for French Orphans; for this the French government decorated him as Chevalier of the Legion of Honor; received also the Medal of the Reconnaissance Française; consulting physician at the Willard Hospital; on the staffs of the New York Foundling and Presbyterian hospitals; died Jan. 19, aged 78, of arteriosclerotic heart disease.

Bass, Mary Elizabeth, Lumberton, Miss.; born in Carley, Miss., April 5, 1876; Woman's Medical College of Pennsylvania, Philadelphia, 1904; an associate member of the American Medical Association; member of the Louisiana State Medical Society; emeritus fellow of the College of American Pathologists; fellow of the American College of Physicians; professor emeritus of medicine at Tulane University of Louisiana School of Medicine, New Orleans; specialist certified by the American Board of Pathology; at one time secretary and vice-president of the Orleans Parish Medical Society; in 1921 president of the American Medical Women's Association and in 1953 was presented with its Elizabeth Blackwell Centennial medal; in 1952 was the recipient of the Alumnae Achievement award of the Woman's Medical College of Pennsylvania; died in New Orleans Jan. 26, aged 79, of abdominal adenocarcinoma.

Bowen, Ralph ✠ Houston, Texas; born in Iowa City, Iowa, July 4, 1898; State University of Iowa College of Medicine, Iowa City, 1924; clinical associate professor of medicine at Baylor University College of Medicine; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; fellow of the American College of Allergists, of which he was a founder and first vice-president; fellow of the American Academy of Allergy and the American College of Physicians; past-president of the allergy section, Southern Medical Association; past-president of the Southwest Allergy Forum; served during World War I; chief of the division of allergy at Texas Children's Hospital; on the staffs of the St. Joseph Hospital and the Methodist Hospital, where he died Jan. 31, aged 57, of myocardial infarction.

Redfield, Robert Ray, Senior Surgeon, U. S. Public Health Service Reserve, Bethesda, Md.; born in Ogden, Utah, July 7, 1923; Johns Hopkins University School of Medicine, Baltimore, 1946; interned at Salt Lake County General Hospital in Salt Lake City; became a research assistant in biochemistry at the University of Utah, Salt Lake City, remaining there until 1948, when he became an atomic energy commission fellow at the University of Chicago, where later he was a U. S. Public Health Service fellow and an instructor in the department of medicine; since 1952 served as research investigator for the laboratory of cellular physiology of the National Heart Institute, U. S. Public Health Service; died Jan. 2, aged 32.

Maertz, William Frank, St. Peter, Minn.; born in New Prague in 1885; University of Minnesota College of Medicine and Surgery, Minneapolis, 1908; member of the Minnesota State Medical Association; served as president of the Scott-Carver Counties Medical Society; at one time practiced in New Prague, where he was mayor from 1920 to 1922; while practicing in North Dakota was state examiner, and from 1915 to 1917 was coroner of Richland County, N. D.; veteran of World War I; in 1907-1908 was police surgeon in St. Paul; served as a member of the staff of state hospitals at Anoka and St. Peter; died Jan. 3, aged 70, of cerebral thrombosis.

Kruger, Alfred Leon ✠ Norfolk, Va.; born in New York City, Feb. 16, 1911; University of Virginia Department of Medicine, Charlottesville, 1935; fellow of the American College of Chest Physicians and governor for the state of Virginia; member of the American Trudeau Society; fellow of the American College of Physicians; a member of the executive committee of the Virginia Tuberculosis Association; specialist certified by the American Board of Internal Medicine; served during World War II; on the staffs of the De Paul and Norfolk General hospitals; died Dec. 25, aged 44, of coronary thrombosis.

✠ Indicates Member of the American Medical Association.

Adams, William Lanier, Fresno, Calif.; Cooper Medical College, San Francisco, 1906; served during World War I; formerly police surgeon; died Jan. 21, aged 75, of cerebral thrombosis.

Aja y Aja, Nicanor ⊕ Barre, Vt.; Universidad Central de España Facultad de Medicina, Madrid, Spain, 1933; served as city physician and health officer; on the staff of the Barre City Hospital, where he died Jan. 15, aged 47, of coronary occlusion.

Baeseman, R. Winfield ⊕ Interlaken, N. J.; University of Louisville (Ky.) School of Medicine, 1927; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; on the staff of the Fitkin Memorial Hospital in Neptune; died in Bandah, India, Feb. 1, aged 59, of a heart attack, while on his 10th tour of duty at the Church of Scotland Mission.

Bine, Rene, San Francisco; University of California Medical School, San Francisco, 1903; an associate member of the American Medical Association; served on the faculty of his alma mater; a founder of the San Francisco Tuberculosis Association; for many years secretary of the San Francisco Medical Society; on the staffs of the French, Children's, University of California, and Stanford University hospitals and the Mount Zion Hospital, where he died Feb. 14, aged 73, of carcinoma of the stomach.

Bishop, Albert Henry, Dunnell, Minn.; Chicago Homeopathic Medical College, 1900; died in the Holy Family Hospital, Estherville, Iowa, Jan. 4, aged 83, of prostatic hypertrophy and uremia.

Blackwell, Oscar L. ⊕ Chattanooga, Tenn.; Chattanooga Medical College, 1901; commissioner of the East Brainerd utility district; died Jan. 19, aged 81, of a heart attack.

Blaney, Cyril Arthur ⊕ Westford, Mass.; Boston University School of Medicine, 1902; chairman of the board of health; formerly school physician; died Jan. 18, aged 76.

Blim, Spencer Phelps ⊕ Chicago Heights, Ill.; Chicago College of Medicine and Surgery, 1916; served during World War I; on the staff of St. James Hospital; died Jan. 25, aged 62, of cerebral hemorrhage and right hemiplegia.

Bordley, James, Jr. ⊕ Baltimore; University of Maryland School of Medicine, Baltimore, 1896; member of the American Academy of Ophthalmology and Otolaryngology and the American Ophthalmological Society; fellow of the American College of Surgeons; specialist certified by the American Board of Ophthalmology; chairman, Section on Ophthalmology, American Medical Association, 1920-1921; on the staffs of the Hospital for Women and the Union Memorial Hospital; died Jan. 7, aged 81.

Bosch, Calvin Christian Fredrick, Sibley, Iowa; State University of Iowa College of Medicine, Iowa City, 1928; past-president of the Osceola County Medical Society; died Jan. 3, aged 53, of coronary thrombosis.

Bowers, Henry Wolffe ⊕ Nevada, Iowa; Denver and Gross College of Medicine, 1909; also a graduate in pharmacy; interned at St. Luke's Hospital in Denver; past-president of the Story County Medical Society; past-president of the Nevada Rotary Club and a director of the Nevada National Bank; died Jan. 12, aged 73, of cerebral hemorrhage.

Brothers, James Harvey, Jr., Montclair, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1914; served during World War I; died Jan. 23, aged 67, of coronary thrombosis.

Bryson, Daniel Rice, Bryson City, N. C.; University of Maryland School of Medicine, Baltimore, 1900; for 50 years surgeon of Southern Railways; died Dec. 22, aged 79, of Parkinsonism.

Burian, Jenny ⊕ Sidney, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1933; on the staff of the Sidney Hospital; died Dec. 28, aged 46, of cerebral hemorrhage.

Burrows, John Walter ⊕ Berea, Ohio; St. Louis University School of Medicine, 1932; served during World War II; died in the Community Hospital Dec. 14, aged 50, of dissecting aortic aneurysm.

Capehart, Lovelace Brown, Jr., New York City; Columbia University College of Physicians and Surgeons, New York City, 1931; also a graduate in pharmacy; died Dec. 26, aged 60, of cerebral hemorrhage.

Cerasoli, Michael Florinda ⊕ Barre, Vt.; University of Vermont College of Medicine, Burlington, 1930; fellow of the American College of Surgeons; served during World War I; associated with the Barre City Hospital, where he was past-president of the staff and where he died Jan. 19, aged 57, of amyotrophic bilateral sclerosis.

Charr, Robert Kyun Hyun ⊕ Philadelphia; Jefferson Medical College of Philadelphia, 1931; assistant professor of medicine at his alma mater; specialist certified by the American Board of Internal Medicine; member of the American College of Chest Physicians and the American Trudeau Society; fellow of the American College of Physicians; on the staff of the Jefferson Hospital, where he died Jan. 29, aged 51, of cancer of the liver.

Chodoff, Louis, Philadelphia; Jefferson Medical College of Philadelphia, 1904; an associate member of the American Medical Association; member of the teaching staff at his alma mater; died in the Jefferson Hospital Jan. 26, aged 74, of coronary occlusion.

Cleary, Joseph Patrick, Portland, Ore.; Stanford University School of Medicine, San Francisco, 1940; member of the American Public Health Association and the Oregon Public Health Officers Association; medical director, bureau of health, city of Portland; served during World War II; died in the Providence Hospital Jan. 9, aged 45, of bleeding esophageal varices.

Cleaver, Henry Archer, Wilmington, Del.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; an associate member of the American Medical Association; member of the Medical Society of the State of Pennsylvania and the American Roentgen Ray Society; formerly practiced in Philadelphia, where he was for many years roentgenologist on the staff of the Chestnut Hill Hospital; served during World War I; died in Pennsauken, N. J., Jan. 30, aged 90, of arteriosclerosis and cardiac decompensation.

Comer, Charles William ⊕ Mooresville, Ind.; Indiana University School of Medicine, Indianapolis, 1939; interned at the Indianapolis City Hospital; served during World War II; associated with Comer's Sanitarium in Mooresville; died in St. Vincent's Hospital, Indianapolis, Jan. 11, aged 40, of uremia and pyelonephritis.

Cray, Eugene James, Brandon, Vt.; University of Vermont College of Medicine, Burlington, 1909; member of the Vermont State Medical Society; health officer; served during World War I; died Jan. 4, aged 70, of coronary thrombosis.

Crook, Martin ⊕ Spartanburg, S. C.; University of Virginia Department of Medicine, Charlottesville, 1901; past-president of the Spartanburg County Medical Society; served overseas during World War I; died in the Veterans Administration Hospital, Augusta, Ga., Dec. 21, aged 76, of heart disease.

Dismukes, Henry Dodford, Washington, D. C.; Howard University College of Medicine, Washington, 1921; died Oct. 29, aged 63.

Eames, Manley Hunter, Providence Forge, Va.; Bennett Medical College, Chicago, 1914; member of the Medical Society of Virginia; died in a hospital in Richmond Jan. 11, aged 68, of pulmonary infarction.

Erf, Lowell Ashton ⊕ Philadelphia; Ohio State University College of Medicine, Columbus, 1931; assistant professor of medicine at Jefferson Medical College; certified by the National Board of Medical Examiners; fellow of the American College of Physicians; on the staffs of the Jefferson, St. Joseph's, and Veterans Administration hospitals; died Jan. 30, aged 47, of a heart attack.

Faringer, Howard Reiner, Hollywood, Fla.; Hahnemann Medical College and Hospital, Philadelphia, 1897; died in the Memorial Hospital Dec. 4, aged 79, of cerebral hemorrhage and cerebral arteriosclerosis.

Garland, Roy L., Gloucester, Mass.; Harvard Medical School, Boston, 1903; died in the Addison Gilbert Hospital Jan. 15, aged 77, of cerebral hemorrhage.

Gillman, Robert Winthrop ✠ Detroit; Detroit College of Medicine, 1887; for many years on the faculty of his alma mater; fellow of the American College of Surgeons; served on the staffs of St. Mary's, Woman's, and Providence hospitals; died in the Grace Hospital Jan. 17, aged 90, of bronchopneumonia.

Glover, Charles A., Pine Bluff, Ark.; University of Arkansas School of Medicine, Little Rock, 1904; died Jan. 22, aged 82, of congestive heart failure.

Hill, Howard Gilman, Redlands, Calif.; University of California Medical School, San Francisco, 1903; fellow of the American College of Surgeons; for many years on the board of directors of the Y. M. C. A.; for many years on the staff of the Redlands Community Hospital, where he died Jan. 5, aged 79, of cor pulmonale.

Hinkley, Junie Joseph, Westfield, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1896; died in Paris (Ill.) Hospital Dec. 29, aged 84, of bronchopneumonia, encephalomalacia, and cerebral arteriosclerosis.

Hodge, William Henry, Niagara Falls, N. Y.; Chicago Homeopathic Medical College, 1889; an associate member of the American Medical Association; past-president of the New York and New England Association of Railway Surgeons; a member of the first board of trustees of the Martha H. Beeman Foundation Child Guidance Clinic and for 18 years served as president of the foundation; associated with St. Mary's Hospital and the Memorial Hospital, where he died Jan. 13, aged 90, of bronchogenic carcinoma.

Holt, George Henry ✠ Jamestown, N. D.; Milwaukee Medical College, 1908; on the staffs of the Jamestown and Trinity hospitals; died Dec. 10, aged 76, of coronary occlusion.

Holt, Hiram Allen ✠ Prospect Harbor, Maine; Jefferson Medical College of Philadelphia, 1896; died in Sullivan Dec. 9, aged 87, of myocardial infarction and arteriosclerosis.

Hopkins, James A., Cedar Grove, W. Va.; Meharry Medical College, Nashville, Tenn., 1906; served as councilman and health officer; died Dec. 9, aged 77, of asthma.

Johnston, Rufus O., Gainesville, Fla.; University of Minnesota Medical School, Minneapolis, 1928; an associate member of the American Medical Association; served during World War II; died Dec. 29, aged 54, of coronary thrombosis.

Kadzewick, Joseph William, Chicago; Loyola University School of Medicine, Chicago, 1932; served during World War II; on the staff of the Holy Cross Hospital; died Jan. 26, aged 50, of cancer.

Kaine, William Joseph ✠ Brattleboro, Vt.; McGill University Faculty of Medicine, Montreal, Canada, 1911; served on the staff of the Brattleboro Memorial Hospital, where he died Jan. 26, aged 73, of cirrhosis of the liver.

Kelley, Charles Henry ✠ Washington, D. C.; Howard University College of Medicine, Washington, D. C., 1929; associate professor of radiology at his alma mater; specialist certified by the American Board of Radiology; member of the Radiological Society of North America; fellow of the American College of Radiology; chief of the division of radiology at Freeman's Hospital; died Jan. 17, aged 54, of coronary heart disease.

Kennedy, Kendall Owen ✠ Utica, Ohio; Ohio State University College of Medicine, Columbus, 1937; served during World War II; on the staffs of the Mercy Hospital and the Memorial Hospital in Mount Vernon, where he died Jan. 16, aged 45, of nephritis.

Kerns, Ira Nelson ✠ Louisville, Ky.; Kentucky University Medical Department, Louisville, 1905; fellow of the Industrial Medical Association and the International College of Surgeons; member of the American Academy of General Practice; died in Anchorage Nov. 14, aged 72, of myocardial infarction.

Kime, John Thomas ✠ Petersburg, Ind.; University of Louisville (Ky.) Medical Department, 1889; died in the Good Samaritan Hospital, Vincennes, Dec. 10, aged 89, of cerebral hemorrhage and arteriosclerosis.

King, William May, Oklahoma City, Okla.; Eclectic Medical College, Cincinnati, 1882; died in the Hubbard Hospital Jan. 15, aged 98, of pneumonia and arteriosclerosis.

Kistler, Eugene Monroe, Allentown, Pa.; Bellevue Hospital Medical College, New York City, 1893; for many years on the staff of Sacred Heart Hospital; died Dec. 23, aged 82, of arteriosclerosis.

Klucikowski, Norbert Andrew ✠ Evergreen Park, Ill.; University of Illinois College of Medicine, Chicago, 1943; interned at Grant Hospital in Chicago; member of the Industrial Medical Association and the American Academy of General Practice; served during World War II; on the staff of the Little Company of Mary Hospital, where he died Dec. 16, aged 39, of acute myocardial infarction.

Korkes, Seymour, Durham, N. C.; New York University College of Medicine, 1945; interned at the Queens General Hospital in Jamaica, N. Y.; certified by the National Board of Medical Examiners; associate professor of biochemistry at Duke University School of Medicine; formerly on the faculty of his alma mater; served in the medical reserve corps of the U. S. Army; on the staff of the Duke Hospital; died Dec. 10, aged 33, of injuries received in an automobile accident.

Nutter, Charles Francis ✠ Nashua, N. H.; Medical School of Maine, Portland, 1892; honorary life member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; formerly vice-president of the New Hampshire Surgical Club; served during World War I; on the staffs of the Monadnock Community Hospital in Peterborough and St. Joseph's Hospital and Nashua Memorial Hospital, where he died Dec. 22, aged 85, of carcinoma of the stomach.

Parkes, Charles Herbert ✠ Sharon, Wis.; Rush Medical College, Chicago, 1897; fellow of the American College of Surgeons; died in the Lakeland Hospital in Elkhorn Dec. 10, aged 83, of arteriosclerotic heart disease.

Patrick, Joseph Franklin ✠ Wenatchee, Wash.; University of Louisville (Ky.) Medical Department, 1908; died in St. Anthony's Hospital Jan. 10, aged 71, of myocardial infarction.

Preston, Frank, Binghamton, N. Y.; University of Vermont College of Medicine, Burlington, 1903; an associate member of the American Medical Association; examining physician for the city of Binghamton from 1941 to 1953; on the staff of the Binghamton City Hospital; died in Demarest, N. J., Dec. 3, aged 83, of myocardial infarction.

Price, William Herbert ✠ Charleston, S. C.; Medical College of the State of South Carolina, Charleston, 1911; at one time assistant city bacteriologist and for many years member of the city health department; served on the Mexican border and during World War I; died in the New Roper Hospital Dec. 30, aged 72, of hypertensive cardiovascular disease.

Pyrtle, James Robert, Centerville, Mo.; National University of Arts and Sciences Medical Department, St. Louis, 1918; member of the Missouri State Medical Association; died Dec. 18, aged 71, of coronary thrombosis.

Quigley, Frederic James, Hanover, N. H.; Kentucky School of Medicine, Louisville, 1906; past-president of the Medical Society of New Jersey; member of the American Trudeau Society; past-president of the Hudson County (N. J.) Medical Society; retired medical director of the Berthold S. Pollak Hospital for Chest Diseases in Jersey City, formerly known as the Hudson County Tuberculosis Hospital, where for many years he was a member of the board of managers and president; surgeon, St. Mary's Hospital in Hoboken, N. J.; died Dec. 23, aged 72, of uremia.

Reed, Henry L. ✠ Licking, Mo.; Barnes Medical College, St. Louis, 1904; died in the Baptist Memorial Hospital, Memphis, Tenn., Dec. 20, aged 76, of arteriosclerotic heart disease.

Rieg, John Fred ✠ Detroit; Detroit College of Medicine and Surgery, 1914; died in the Providence Hospital Dec. 26, aged 67, of carcinoma of the colon with metastasis.

Sayre, Harry Clinton ✦ Warwick, N. Y.; New York Homeopathic Medical College and Hospital, New York City, 1905; on the staff of St. Anthony's Hospital; a director of the First National Bank; town and village health officer; school physician; died Dec. 20, aged 72, of metastatic carcinoma.

Scadron, Eugene Nestor, New York City; Duke University School of Medicine, Durham, N. C., 1934; assistant clinical professor of obstetrics and gynecology at the New York College of Medicine; specialist certified by the American Board of Obstetrics and Gynecology; certified by the National Board of Medical Examiners; member of the Medical Society of the State of New York; served during World War II; on the staffs of Mount Sinai and Bellevue hospitals; died Jan. 19, aged 48, of injuries received in an automobile accident.

Season, Edwin Herbert, Covina, Calif.; Western Reserve University Medical Department, Cleveland, 1898; formerly practiced in Cleveland, where he was on the staff of the Lakeside Hospital; died in the Covina Inter-Community Hospital Dec. 22, aged 83, of carcinoma of the bladder.

Shelley, Hilton J., Middletown, N. Y.; Eclectic Medical College, Cincinnati, 1889; an associate member of the American Medical Association; for many years city health officer; died in the Elizabeth A. Horton Memorial Hospital Dec. 24, aged 91, of carcinomatosis and squamous cell carcinoma of the right hand.

Shelton, Norris ✦ Jackson, Tenn.; University of Tennessee College of Medicine, Memphis, 1945; interned at the Atlantic City (N. J.) Hospital; member of the American Academy of General Practice; served in the medical reserve corps of the U. S. Army; died Dec. 18, aged 36, in an automobile accident.

Sine, Arnot Crawford ✦ Lieut. Colonel, U. S. Army, Silver Springs, Md.; State University of Iowa College of Medicine, Iowa City, 1941; interned at the Dr. W. H. Groves Latter-Day Saints Hospital in Salt Lake City; formerly a resident in pathology at Fitzsimons General Hospital in Denver; served during World War II; died Jan. 1, aged 41.

Slavin, Joseph Edward, Waterbury, Conn.; University of Vermont College of Medicine, Burlington, 1912; member of the Connecticut State Medical Society; on the staff of St. Mary's Hospital; state athletic commission boxing physician; died Dec. 16, aged 72, of coronary occlusion.

Smoczynski, Mieczyslaw Edward, Mount Carmel, Pa.; Jefferson Medical College of Philadelphia, 1917; interned at St. Agnes Hospital in Philadelphia; served during World War I; a member of the Selective Service Board of the Mount Carmel District during World War II; formerly school physician; at one time practiced in Philadelphia, where he was affiliated with Oncologic Hospital and Jefferson Hospital; died in the Geisinger Memorial Hospital, Danville, Dec. 31, aged 62.

Sorrells, John Ennis ✦ Lake Charles, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1932; member of the International College of Surgeons; on the staffs of the Memorial Hospital and St. Patrick's Hospital, where he died Dec. 27, aged 47, of acute myocardial infarction.

Staats, Okey Maxwell, Wheeling, W. Va.; Detroit College of Medicine, 1904; served during World War I; an associate member of the American Medical Association; on the staff of the Ohio Valley General Hospital, where he died Jan. 25, aged 78, of coronary thrombosis.

Suffoletta, Daniel Benedict ✦ Midland, Pa.; Jefferson Medical College of Philadelphia, 1931; interned at St. Francis Hospital in Pittsburgh; member of the American Academy of General Practice; served during World War II; on the staffs of the Rochester (Pa.) General Hospital and the Providence Hospital in Beaver Falls; councilman; director of the First National Bank; died in St. Petersburg Beach, Fla., Dec. 3, aged 51, of coronary occlusion.

Taylor, William Ray, The Dalles, Ore.; Northwestern University Medical School, Chicago, 1912; served during World War I; medical officer of the Wasco-Sherman Public Health Department; on the staffs of The Dalles General Hospital and the Mid-Columbia Hospital, where he died Dec. 19, aged 69, of coronary occlusion.

Tritsch, John Edgar, Pelham, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1918; clinical professor of obstetrics and gynecology at his alma mater; member of the Medical Society of the State of New York; fellow of the American College of Surgeons; veteran of World War I; on the staffs of the Metropolitan and Flower and Fifth Avenue hospitals in New York City; died in the New Rochelle (N. Y.) Hospital Jan. 4, aged 61, of cirrhosis of the liver.

Turrill, Vernon Le Verne, Tulsa, Okla.; University of Toronto Faculty of Medicine, Toronto, Canada, 1909; served in the Canadian Medical Corps during World War I; died Jan. 26, aged 74.

Uzzell, Edward Foy ✦ Atlantic City, N. J.; Jefferson Medical College of Philadelphia, 1916; fellow of the American College of Surgeons; past-president of the Atlantic County Medical Society; served overseas during World War I; chief obstetrician and gynecologist at the Atlantic City Hospital; died Jan. 21, aged 63, of acute coronary occlusion.

Vogt, Walter Eugene, Jr. ✦ Brooklyn, N. Y.; Cornell University Medical College, New York City, 1937; served during World War II; member of the American Academy of General Practice; on the staffs of the Evangelical Deaconess and Queen General hospitals; died in East Williston Dec. 12, aged 44, of coronary atherosclerosis.

Vohr, Dorothy Ruth Larrison ✦ Lee, Mass.; Middlesex University School of Medicine, Waltham, 1932; served during World War II; died Dec. 14, aged 49.

Webb, William C. ✦ Disputanta, Va.; University of Maryland School of Medicine, Baltimore, 1904; county medical examiner; chairman of the board of welfare, and member of the finance board; surgeon for the Norfolk and Western Railroad; on the staff of the Petersburg (Va.) General Hospital, where he died Jan. 2, aged 76, of cerebral thrombosis.

White, Paul Amos ✦ Davenport, Iowa; George Washington University School of Medicine, Washington, D. C., 1916; entered the Mayo Foundation in Rochester, Minn., in 1917; fellow of the American College of Surgeons; past-president of the Scott County Medical Society; a deputy councilor for the 11th Councilor District of the Iowa State Medical Society; served as president of the staffs at Mercy and St. Luke's hospitals; in 1946 appointed to the National Advisory Board of Stephens College, Columbia, Mo.; died Dec. 25, aged 71, of lymphosarcoma.

Wick, Victor V., Santa Ana, Calif.; Jefferson Medical College of Philadelphia, 1900; died in the Santa Ana Community Hospital Nov. 29, aged 79, of coronary thrombosis.

Williamson, Cordelia Isabella MacNaughton ✦ San Diego, Calif; Tufts College Medical School, Boston, 1912; member of the Massachusetts Medical Society; died Dec. 13, aged 78, of cerebrovascular accident.

Witcpalek, William Wencel ✦ Kewaunee, Wis.; Northwestern University Medical School, Chicago, 1911; died in St. Vincent's Hospital, Green Bay, Dec. 7, aged 84, of chronic myocarditis and arteriosclerosis.

Wulp, George Adolf ✦ Hartford, Conn.; University of Michigan Medical School, Ann Arbor, 1930; fellow of the American College of Physicians; served during World War I; on the staffs of the Hartford Hospital and St. Francis Hospital; consultant at the Newington (Conn.) Home and Hospital for Crippled Children; consulting internist, State of Connecticut Veterans' Home and Hospital; a staff member of the University of Connecticut in Storrs, and a trustee of Hillyer College; died Jan. 1, aged 59, of acute myocardial infarction.

Wycislik, John Parma ✦ Cleveland; Western Reserve University School of Medicine, Cleveland, 1919; member of the Cleveland Academy of Medicine; on the staffs of the Grace and Evangelical Deaconess hospitals and the Marymount Hospital, where he died Jan. 1, aged 70, of cancer.

Young, Evelyn Nancy, Effingham, Ill.; Jenner Medical College, Chicago, 1913; worked for many years for the board of education of Chicago; died in St. Anthony's Memorial Hospital Jan. 19, aged 78, of carcinoma of the liver and coronary atherosclerosis.

FOREIGN LETTERS

AUSTRIA

Thrombopenia with Aplasia of Radius.—At a joint meeting of the Austrian Society of Gynecology and Obstetrics and the Society of Pediatrics on Jan. 10, Dr. H. Gross reported on four patients in whom congenital hypoplastic thrombopenia was combined with bilateral congenital aplasia of the radius. It is not likely that this concurrence of defects is accidental. Two of the speaker's patients are siblings. The first of these is 19 years old and shows marked debility. This patient had two operations, which were completed without complications, but even today the thrombocyte count in this patient is only 18,000 per cubic millimeter. Two other patients have not yet been operated on for their hemorrhagic tendency. The fourth child died shortly after birth as the result of a Treitz hernia.

Neonatal Metabolism and Renal Function.—At the same meeting, H. A. McCance and E. M. Widdowson stated that observations on infants in their first two days of life revealed that, if they are healthy, have been carried to term, and are deprived of food, they derive their basic calories to a much smaller extent from the decomposition of tissue proteins than do fasting adults. They also found that the volume of urine (expressed in units of body fluids) excreted by healthy infants who have been carried to term is the same as in adults who have been subjected to comparative deprivation of food and fluid. The urine of the infants differed in that it had a much lower osmotic total concentration. The osmotic concentration of the urine of the infants showed the same composition as that of the urine of adults, except that the potassium content was higher. Infants who had been carried to term and those who had been carried beyond term, and who had had a long and difficult delivery, showed an increased decomposition of body protein, a reduced glomerular filtration speed, an inadequate clearance of urea, a reduced urinary volume, a higher nitrogen-potassium ratio in the urine, and an elevated excretion of inorganic phosphates. The renal function of prematurely born infants was the same as that of infants who had been carried to term. The kidneys of the prematurely born infants had the same capacity to hold the serum urea content within normal limits as did the kidneys of infants carried to term, and their protein metabolism also was the same. Two very tiny infants, who died, had a high protein catabolism, a very poor renal function, and comparatively high quantities of sodium in the urine. These results, if confirmed, should interest pediatricians and gynecologists as well as all those who are interested in intrauterine life processes, because the postnatal functions examined are the result of processes that took place in the last hours or days the fetus was within the uterus.

Terebrating Carcinoma.—At the Dec. 16 meeting of the Society of Physicians of Vienna, Dr. A. Matras applied the term terebrating carcinoma to basal cell cancers involving chiefly the skin of the scalp and forehead that progress insidiously and are characterized by great resistance to therapy and by unlimited extension in both surface and depth. Healing was achieved in a 67-year-old woman with this disease by surgical extirpation, evisceration of the orbit, and plastic repair. In another patient, a woman aged 63, the growth was arrested from 1942 to 1951 by radium irradiation but then infiltrated the cranium down to the dura mater. This form of cancer urgently requires early radical surgical treatment with complete removal of the cancerous tissues and plastic repair if the growth cannot be arrested by irradiation.

Roentgenography of the Bile Passages.—At the same meeting Dr. H. Brücke of Mürzzuschlag said that the use of Biligrafin makes possible visualization not only of the gallbladder but also of the larger bile ducts. This is of greatest importance in patients in whom disorders remain after cholecystectomy. Roentgenologic procedures as well as manometry should be used during the exploration of the deep bile passages, as they reveal otherwise missed stones in the ductus choledochus and in the hepatic bile passages and cicatricial inflammatory stenosis in the region of the duodenal papilla and of the intrapancreatic portion of the ductus choledochus. Observations of several hundred patients show that with these aids the operation becomes much more accurate and effective and the prospects for complete freedom from symptoms are greatly increased. No matter how thorough the exploration with the methods formerly available, roentgenologic and manometric examination during the operation should not be omitted. The term "postcholecystectomy syndrome" should be discontinued because the condition so described is not really a syndrome and is not a direct result of the removal of the gallbladder. Postoperative symptoms have many causes and only part of them can be traced to the bile passages. The already favorable results in cholelithiasis and cholecystitis (75 to 80% obtain complete freedom from symptoms) can be further increased by more exact diagnosis, early operation in every case, and the routine use of roentgenologic methods and determination of biliary pressure.

BRAZIL

Gas Gangrene.—According to Dr. Genesio Pacheco in *Memorias do Instituto Oswaldo Cruz*, gas gangrene has usually been considered a local infection with systemic symptoms. Its central nervous system symptoms are similar to those of tetanus and botulism. It is likely therefore that the gas gangrene toxin is neurotropic. Dr. Genesio Pacheco and his co-workers demonstrated lesions in the central nervous system of animals that had been exposed for varying lengths of time to gas gangrene toxin. In acute intoxication after intracranial inoculation, severe damage occurred within 20 to 30 minutes in the cells of the spinal cord, especially in motor cells, and also in some cells of the posterior cord and medulla oblongata. The lesions were chromatolytic and pyknotic and were most marked in animals exposed to Clostridium histolyticum and Cl. perfringens toxins. The myelin sheath remained intact. In delayed poisoning with larger and repeated doses, lesions of the brain, medulla oblongata, and spinal cord were observed. These lesions were characterized by hyperemia, perivascular hemorrhages in the white and grey matter, edema, accumulation of glial cells with enlarged and hyperchromatic nuclei, and fragmentation of the myelin sheath. Changes found less often included agglutination of Nissl bodies, sinuous appearance of the dendritic endings, and neuronophagia around "ghost" cells. These workers showed that nervous fibers exposed to these toxins lost their conductive ability even before significant lesions developed. Since the myotoxic action of the poisons would not explain the rapid death observed in most patients with gas gangrene nor the sudden appearance of distressing symptoms, the authors conclude that gas gangrene is primarily a neurotoxic disease.

Dr. Adolfo Lutz's Centennial.—On Dec. 18, the 100th anniversary of the birth of Dr. Adolfo Lutz, who died in 1940, was commemorated in Brazil by biologists, parasitologists, entomologists, bacteriologists, mycologists, zoologists, veterinarians, and others concerned with public health. The laboratory of the São Paulo State Department of Health published a special issue of *Revista do Instituto Adolfo Lutz* (vol. 15, 1955). The complicated biology of the trematodes Australorbis glabratus and Tropicorbis centimetralis and their development in the mollusk were first described by Lutz, who founded the first Brazilian school of microbiology. Lutz was also the first physician to diagnose cholera and plague in Brazil, both having been brought into the country from Europe. South American blastomycosis caused by Blastomyces brasiliensis is still known as Lutz's disease.

Ascariasis.—Drs. Vicente Amato Neto and Marcelo Corréa treated 54 patients suffering from ascariasis with piperazine hydrate using a daily dose of 60 mg. per kilogram of body

The items in these letters are contributed by regular correspondents in the various foreign countries.

weight; 22 patients received the drug for five days; 28 for seven days; and the remaining 4 received two courses for seven days, separated by a seven-day interval. The percentage of cures for these three groups was 63.63, 89.28, and 100.0 respectively. In an article published in *Revista do Instituto Adolfo Lutz* (vol. 15, 1955), the authors stated that piperazine hydrate is one of the most efficacious therapeutic agents for ascariasis. Its advantages are that (1) it is almost completely nontoxic, (2) no special precautions are needed in its administration, (3) it may be given easily to infants, and (4) it is cheap.

COLOMBIA

Cancer.—In *Antioquia Medica* (vol. 5, pages 589-605) Dr. P. Correa Vélez said that, of 10,400 autopsies done from 1944 to 1951, cancer was reported in 2,557 (975 in men and 1,568 in women; in 14 the sex was not stated). The frequency of cancer in organs that are common to both sexes was about equal for men and women. The youngest patient was a 2-month-old girl with a congenital sarcoma of the knee, and the oldest was a 105-year-old man with a basal cell carcinoma of the skin. The average age for patients with cancer was 49¼ years. The most frequent form was cancer of the skin; it appeared in 22.68% of the total number, with an average age of the patients of 74 years.

Centers of Public Assistance.—The Federal Department of Statistics reports that, of the total number of institutions for public assistance, 39% are official, 20.2% are semiofficial, and 33.7% are private; the status of the rest is unknown. The proportion of beds for the medically indigent is 83.4%. In view of the high rate of infant mortality (103 per thousand infants born alive in 1954), the facilities for infant care are disproportionately small.

DENMARK

Ornithosis.—Denmark has recently shown an increasing incidence of ornithosis. Jörgensen and Steffensen in the *Danish Medical Bulletin* for February, 1956, suggest that this may partly be due to an increase in the importation of psittacine birds since 1952. Some of the patients in their series of 44 gave no history of contact with birds, and in none could contact with another human having ornithosis be demonstrated. None of the patients died of ornithosis, and the severe clinical findings noted in earlier accounts of the disease were rarely seen. The disease usually began suddenly with chills and a rise of temperature to 39 or 40 C (102 or 104 F) in one or two days. A high fever persisted for about a week, after which it fell by lysis. The temperature curve often ended in a prolonged subfebrile course. Secondary bouts of fever and relapses were frequent. During the initial stage, the patients complained of headache and various other aches and pains. A slight sore throat and nasal congestion were often followed after a few days by a dry, nonproductive cough. Ornithosis is becoming common in Copenhagen. As the demonstration of the virus from the patients was not practicable, the chief diagnostic criterion was a positive complement-fixation test. Certain related diseases may also give a positive reaction, but, as they are never seen in Denmark, this was of no importance. The treatment given was not very satisfactory, and it would seem that the sulfonamides are probably of no use against this disease. On the other hand, penicillin and chlortetracycline had a favorable but not very striking effect. The x-ray findings showed patchy infiltrations consistent with pneumonitis. In a few instances roentgenographic changes did not develop till after the 14th day of the illness.

Morphine Poisoning.—Dr. Mogens Nimb in *Ugeskrift for læger* for Jan. 19, 1956, states that, although the number of patients with barbiturate poisoning alone has shown a marked increase in the last few years, the number of patients with morphine poisoning has remained remarkably constant since 1949. In 55% of a series of 145 patients, the drug was taken with suicidal intent. In the entire series there were 73 cases of pure morphine poisoning and 72 of combined morphine and barbiturate poisoning. In many of the 19 patients who died, death was largely due to paralysis of the respiratory system, but in only 2 of these cases was such a paralysis the direct cause of death. In all six of the patients whose death was due to shock, a barbiturate in addition to the morphine had been taken. Nimb insists that the old treatment of morphine poisoning with stimulants is irrational since the introduction of specific antidotes for morphine poisoning. On the other hand, he attaches great importance to relief of respiratory embarrassment by keeping the respiratory passages clear. In 23 patients artificial respiration was given; whereas, 43 recovered when oxygen inhalation through a catheter was used without artificial respiration. Shock was observed in 20 patients, but in only 10 was it so great as to require intravenous injections.

School for Medical Secretaries.—It has been thought for some time that medical secretaries would do their work better and enjoy a better status if they were given special training followed by an examination yielding a certificate of proficiency. With this aim in view and in order to achieve a less haphazard mode of selecting such secretaries, a group of physicians and secretaries worked out an eight-month course, which has proved useful. The first class was started in 1954 when 25 selected applicants began their training. Classes were held from 3 to 6 p. m. Monday through Friday. A minimum age of 21 was agreed on. The curriculum included such clerical work as stenography, typing, accounting, and filling in hospital records and such special subjects as anatomy, physiology, pathology, medical nomenclature, case recording, and laboratory tests. In May, 1955, 23 of the 25 scholars satisfactorily completed the course. Juniors (those having no experience as medical secretaries) and seniors (those with some previous experience) were taught separately in the class beginning in August, 1955. The training is to last 10 months instead of 8, and altogether 570 hours are to be devoted to the training, which will include visits to hospitals. Medical Latin will also be taught.

FRANCE

Hormonal Treatment of Tuberculosis.—The hormonal treatment of tuberculous serofibrinous pleurisy has given good results according to a number of researchers. In 1954 M. Cachin and his co-workers in *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* (page 443) reported accidents due to this treatment. Intrapleural administration of hydrocortisone in a patient with pleurisy on the right caused perforation of the visceral pleura and microscopic lesions. The authors concluded that hormonotherapy is contraindicated when a parenchymatous lesion is associated with tuberculous serofibrinous pleurisy. Moreau and Besançon reported to the same society in October, 1955, the case of a 20-year-old woman who was given 10 mg. of corticotropin intravenously for a tuberculous serofibrinous pleurisy that was not influenced by antibiotics. A perforation occurred, but fortunately the consequences were not serious. They propose a very cautious administration of 10 mg. of corticotropin over a period of 12 hours every second day for 10 days. This method of treatment is effective and has not as yet been associated with any accidents.

Tuberculous pericarditis, formerly always fatal, can now be treated with antibiotics and cured, but this cure is likely to result in a constrictive pericarditis. For this reason, corticotropin and cortisone have been added to the usual treatment. Y. Bouverain and his co-workers reported to the same society in November, 1955, the results in three patients treated in this way. In the first patient they were able to inject 25 mg. of hydrocortisone into the pericardial sac. In the other two, in addition to antibiotics, they gave 12.5 mg. of corticotropin and 50 mg. of hydrocortisone for three or four weeks. The patients were followed five to seven months and showed no signs of adiastole.

Diverticulosis of the Small Intestine.—In "Encyclopédie médico-chirurgicale" (1955), M. Carabolona stated that simple diverticulosis of the small intestine is characterized radiologically by either pediculate images that are opaque when the patient is lying down and partly transparent when he stands or by residual

images resembling bunches of grapes or pigeons' nests. The clinical syndrome is variable, with vague pains, rumblings, diarrhea or constipation, nausea, and tympanites. There are three groups of complicated diverticulosis: (1) subacute, with bouts of diarrhea; (2) acute, resembling appendicitis and especially likely to settle around the umbilicus or in the left lower abdominal quadrant; and (3) pseudotumoral, resulting from inflammation of the mesenteric lymph nodes. Diverticular tumors are rare, but diverticulosis can give rise to a mechanical occlusion, hemorrhage, or perforation. The treatment of simple diverticulitis is medical, but, if complications are present, it should be surgical. M. Hardonni in the same issue said that pain, constipation, fever, and especially signs of bladder irritation and a mass in the left iliac region (capable of regression) are characteristic of diverticulosis, while hemorrhage, emaciation, and a fixed tumor in the left iliac region are typical of cancer.

Operation in Lung Abscess.—Sauvage (Encyclopédie médico-chirurgicale, 17th Notebook on Therapy, 1955) says even the most conservative lung operations entail some risk, but success is usual if good postoperative care is practiced. The most important point, however, is careful selection of patients. Only a few can be benefited by operation. Only rarely should a pulmonary abscess be treated surgically, since most of these respond to medical treatment, provided it is instituted early. Antibiotics are the best treatment. Operation is justified in 10 to 30% of cases, specifically those with persistent suppuration, hemoptysis, or relapse caused by a residual lesion that has been verified by radiological examination. Radical pneumonectomy does not have to be performed as often as in the past, because of better medical treatment, and its results are better, because of improved preparation of the patients. Segmental resection is the most benign operation when practiced for the proper indications. Lobectomy remains the most frequently used procedure, and the more careful the selection of patients and the better the preoperative preparation, the better its results.

Malignant Cardiac Rheumatism.—P. Grenet and M. Caramanian (Encyclopédie médico-chirurgicale, Notebook 322 on Infectious Diseases, 1955) fixed the age of children with rheumatic fever that is malignant immediately or after a first attack at 7 years. The onset may be violent or insidious. The signs of malignancy are stubborn pyrexia, a highly accelerated pulse, low output of urine, extreme pallor, torpor or agitation, significant dyspnea, enlarged painful liver, splenomegaly, digestive disorders, and arthralgia. The prognosis depends on the amount of myocardial involvement. The commonest signs are tachycardia, even without hyperthermia; dull bruits; gallop rhythm; apical systolic murmur; and preventricular murmur. Ventricular tachycardia, as revealed by electrocardiography, is the worst prognostic sign. The disease may develop in any of a number of ways: superacute forms; severe forms with slow development, sometimes with Streptococcus viridans in the blood culture; or protracted forms, with incomplete remissions and death occurring in 18 months or two years. The authors think that hormonal therapy may be successful in the last cases.

Psychic Disturbances and Osteitis Deformans of Skull. — In *Journal de médecine de Lyon,* Oct. 5, 1955, J. Dechaume and L. Bourrat reported on three patients with osteitis deformans (Paget's disease) of the skull accompanied by psychic symptoms. The findings conflict with Sir James Paget's statement that the minds of these patients remain unaffected no matter how great the extent of bone deformity present. The literature yielded about 40 more cases in which mental disturbance dominated the clinical picture. The symptoms can be divided into three groups: (1) those due to constitutional weakness or manic-depressive psychosis, possibly unrelated to the disease; (2) those resulting from a syndrome of anxiety and hypochondria, due in part to progressive deafness; and (3) those caused by atrophy of the brain (the authors report a case of dementia appearing early in a patient with undiagnosed osteitis deformans in whom cerebral atrophy was demonstrated).

Methyl Bromide Poisoning.—Methyl bromide is widely used in fire extinguishers, refrigerators, insecticides, and rodenticides, and reports of fatal poisoning with this product have been increasing. A. Corcos and his co-workers reported to the Medical Society of Paris Hospitals in October the case of a 43-year-old man employed in an insecticide plant, who, several hours after having poured 800 kg. of methyl bromide into a vat, had convulsive seizures lasting 5 or 10 minutes and coming on every 15 or 20 minutes. The seizures were characterized by clonic movements of the extremities and rolling of the eyes, but there was no loss of consciousness or sphincter control. Twenty-four hours later he was unable to elevate his arm or turn his neck. Melena, black vomitus, and hematomas at the sites of injections were observed, and the patient died of acute pulmonary edema.

Tonsillectomy and Inflammatory Rheumatism. — F. Coste and his co-workers (*Rev. rhum.* **22:**618, 1955) named three types of rheumatism in which a rhinopharyngeal infection may play a part: chronic inflammatory rheumatism, rheumatic fever, and postanginal infectious rheumatism (usually caused by streptococci). In the first two, antibiotics and tonsillectomy generally fail to cure, but the reverse is often true for certain postanginal cases in which the development seems directly linked to infection of the tonsils. When the persistence of tonsillitis and its infecting role are in doubt, the coincidence of an increased number of serum antistreptolysins and favorable results of antibiotic treatment is an indication that tonsillectomy will produce a good result.

Surgeon's Responsibility.—An older man was operated on in a clinic. A nun, under the order of the surgeon, gave the patient a cardiac tonic intramuscularly, and the needle injured the left radial nerve, causing paralysis of the arm. The surgeon refused to be held responsible for the accident, as the nun was not employed by him but by the clinic. The court rejected this argument and ruled that, in the operating room, the surgeon has complete authority and must take full responsibility.

Dietary Deficiency and Recourse to Alcohol.—P. Delore and H. Berry (*Presse médicale,* Nov. 19, 1955) showed dietary deficiency causes rats to take to drink. This effect is also noticeable in the human being. Alcoholics with good appetite, good digestion, and normal diet are in a better position to resist intoxication than their fellows without such qualifications. Therefore, a rational diet is of prime importance in the prevention of alcoholism and in better tolerance of alcoholic beverages.

Local Hyperemiants in Arteritis.—René Leriche wrote in *Presse médicale* of Nov. 9, 1955, that patients with arteritis, inclusive of those about to be operated on, those who have been operated on, and those who are not going to be operated on, are better treated by local methods such as intra-arterial injection of procaine or sympathetic block than by general vasodilators.

INDIA

Vaginal Carcinoma.—Dutta Chaudhari R. in the *Journal of the Indian Medical Association* (**26:**1 [Jan. 1] 1956) reported his observations on 20 patients with primary carcinoma of the vagina. The ratio of vaginal cancer to cancer of the cervix was 1:85. The average age of the patients in this series was 54 years, and the average age at which their menopause started was 44.5 years. Four patients were premenopausal, but their last confinement had occurred 11 or 12 years earlier. All patients except four were multiparous (two nulliparous and two uniparous). The commonest symptoms were leukorrhea and vaginal bleeding of two months' to five years' duration. The location of the tumor was predominantly on the posterior vaginal wall. It spread lengthwise and more toward the vault than toward the vulva. The tumors could be divided grossly into four types: proliferative, ulcerative, nodular, and infiltrative. Histologically, they could be classified as adenocarcinoma, epidermoid carcinoma, squamous carcinoma, and anaplastic carcinoma. The most frequent pathological grading was toward the less differentiated variety. The gross and histological types showed no relation.

Carcinoma of the Breast.—Goyal and Gupta in the *Indian Practitioner* (**8:**1095 [Dec.] 1955) state that carcinoma of the breast differs in different places in regards to incidence, age distribution, and relative frequency of various histological varieties. In their

series of 912 microscopically verified cases of malignant disease of both sexes, there were 69 cases of carcinoma of the breast (8% of the entire series and 15% of the female patients). Of 96 tumors of the breast, 69 were malignant. Carcinoma of the uterus was nearly twice as common as carcinoma of the breast. Five of the cases of mammary carcinoma occurred in men, and in 15 the patients were below the age of 35. The encephaloid type was three times as common as the scirrhous variety. The series also included two cases of fibroadenoma undergoing a carcinomatous change, which is a rare transformation.

New Local Anesthetic.—Arora and Sharma in the *Indian Practitioner* (**8**:1101 [Dec.] 1955) state that the comparatively short duration of action of procaine as a local anesthetic even in maximal dose has been a drawback, although its low toxicity has made it one of the most popular local anesthetics. Many new synthetic agents have been tried, but few survived, because their enhanced potency was accompanied by increased toxicity. Trimethylene diurecaine has a broad spectrum of useful local anesthetic activity and a wide margin of safety, but it is ineffective as a surface anesthetic. For infiltration anesthesia, however, it is twice as potent as procaine and has the same penetrating power. It is superior to procaine as a spinal anesthetic and causes less tissue reaction locally.

Amebic Infections.—Mathew and his co-workers in the *Journal of the Indian Medical Association* (**26**:13 [Jan. 1] 1956) reported a survey of the intestinal amebas in 503 patients in a hospital. Seventy patients were suffering from intestinal disorders when admitted to the hospital. Stools were examined every day for a week. The percentage of infection by Endameba histolytica was found to be only 3.8, while that by E. coli was 17.5. Of the 70 patients suffering from intestinal disorders, the incidence of the two infections was 7.1 and 21.4% respectively. Iodameba buetschlii and Endolimax nana were found only rarely.

ITALY

Congress of Industrial Medicine.—The 20th National Congress of Industrial Medicine took place at Padua and Venice in September. Speaking on air pollution, Professor Vigliani said that at Milan an average of 15 tons of solid residue per square kilometer per year is deposited from the air. He urged that steps be taken to reduce this hazard. Professor Saffiotti of Chicago said that the increase in pulmonary cancer, seen especially among men, shows a correlation with the degree of urbanization and industrialization of the area in which the victims live. Chemical studies of the polluted air have led to the identification of compounds noted for their carcinogenic action, and studies with experimental animals have shown the cumulative effect of small doses of carcinogens. There is a correlation between the total dose of the substance and the induction of tumors, but a latent tumor may be activated by small doses, especially if other predisposing factors are present. In addition, there is a synergism in the activity of the carcinogens, even when they are given by different routes. Professor Maugeri of the University of Padua distinguished four stages in the development of silicosis: (1) reduction of the respiratory reserves, resulting in dyspnea without anoxemia; (2) changes of the internal respiration, resulting in dyspnea with anoxemia; (3) reduction of the pulmonary capillary bed, resulting in hypoxemia with hypertension of the lesser circulation; and (4) extensive anatomic reduction with a retardation of the lesser circulation, resulting in irreversible hypoxemia. Hypoxia of the tissues is also frequent as a result of coronary insufficiency. The existence of a myocardial deficit is an important factor, which should be evaluated in all silicotic patients.

Psychological Tests and Myopathies.—At the meeting of the Filippo Pacini Medical Academy of Pistoia in November, Professors Mattioli and Carta reported on certain psychological tests conducted on patients with lipofibrocalcareous myopathy who showed psychic changes. The two tests applied were the profile scale of Vermeylen and the Rorschach test. These were considered as auxiliary to the clinical data and not as purely diagnostic measures. The four patients examined had previously been studied clinically, and biopsy specimens had been taken. The Vermeylen profile could be applied to only three of the patients, because one refused to submit to the test. In these three patients the curve obtained was that shown by mildly disturbed subjects. The Rorschach test revealed fundamental signs of weakness and disharmony in the personality, especially evident in two patients. In the third, constriction of the inner responsiveness predominated over the rest of the elements that made up the personality, but even in this patient signs of weakness and disharmony of the personality itself appeared. In the fourth patient, whose myopathy had been active for about 20 years, the Rorschach test disclosed a mental dissociation suggestive of but not pathognomonic of the terminal phase of schizophrenia. In this patient signs suggestive of organic lesions did not appear, although they had been revealed in the other three. The data obtained from the psychological tests corroborated the clinical observations of these patients.

PERU

Nonfunctioning Tumors of the Adrenal Gland.—In *Archivos peruanos de patologia y clínica*. (vol. 9, no. 4, 1955), Dr. Oscar Urteaga states that little has been written about nonfunctioning primary malignant tumors of the adrenal gland in contrast to the functioning tumors or those with hormonal activity. His series consisted of 14 men, aged 53 to 76 years, who clinically exhibited either an abdominal syndrome, characterized by abdominal pain and a physically noticeable tumor, or a typical mediastinal syndrome, depending on whether the principal metastases from the primary tumor were located at the liver or the mediastinum. The time of onset could not be determined, because the development of the primary tumor was not accompanied by symptoms except in one patient in whom palpation revealed an adrenal tumor in the left flank. Once the metastatic syndrome started, death usually occurred in one to five months, but three patients gave a history of symptoms lasting 12 to 18 months. The primary tumor is usually very small, and in 25% of the patients it reached a diameter of only a few millimeters. Because of this, these tumors may be missed in a routine autopsy. Bony metastases were found to a variable extent in all the patients examined radiographically. Although some patients had renal metastases, such involvement did not cause clinically manifest disturbances. In seven of the patients, a primary tumor was present in both adrenal glands. All of these showed the mediastinal syndrome. In three patients, while one adrenal gland showed evident tumor formations, the other was found to have incipient lesions consistent with the so-called carcinoma in situ. The nature of the underlying adrenal tumors was found on autopsy or biopsy to be cortical carcinoma in four patients, paraganglioma in five, and sympathicoblastoma in five. For the sake of comparison, the author describes four adult patients with benign adrenal tumors and two children with malignant tumors. Of these six tumors, two were functioning (one of these was a cortical carcinoma producing a virilizing adrenogenital syndrome in a 3-year-old girl, and the other was a pheochromocytoma in an adult patient with the typical syndrome of paroxysmal hypertension). The author maintains that the criterion of malignancy for all of these tumors cannot simply be based on the grade of cellular atypia found. For instance, in a patient with relapsing benign adenoma showing frankly atypical cellular islets, the clinical course was benign. On the other hand, most cortical carcinomas and malignant sympathicoblastomas, in spite of showing no cytological evidences of malignancy, give rise to widespread metastases and kill the patient after a brief period. These tumors must therefore be regarded as malignant only if they invade the capsule of the gland or produce metastases.

Social Welfare and the Medical Association.—The Peruvian government's approval of an Employee's Social Welfare Law, which, among other things, monopolizes medical care and hospitalization, extends the benefits of medical insurance to the employee's family, and excludes representatives of the Peruvian Medical Association from the executive committee that will manage this social welfare agency, has moved the Peruvian Medical Asso-

ciation to issue a firm protest and to threaten to strike if the law is enacted. A special commission visited Gen. Manuel. A. Odría, Peru's President, and urged a square deal. The President assured the physicians that their demands would be met and that the medical association would be duly represented in all official committees having to do with the medical care of the insured. The committee initiated a campaign to get all physicians to sign an agreement that they would not cooperate with the Employee's Social Welfare Agency until the proposed law was redrafted to meet their basic demands. At a later meeting of the organizing board of the Employee's Social Welfare Agency, however, the President's delegate disavowed the President's promises and denied that the President had actually meant to imply the promises attributed to him. The final outcome is still in doubt.

SWEDEN

Medical Certificates for Policemen.—The police of Stockholm were agitating last summer for better pay (THE JOURNAL, Oct. 1, 1955, page 509). Several hundred of them and about 100 policemen in Göteborg were reported on the sick list. Since no epidemic disease was present in the rest of the community, it was evident that there was collusion between the policemen and the physicians who issued the medical certificates. An investigating commission reported that four physicians issued certificates of ill health to 81, 33, 51, and 82 policemen respectively. In the opinion of the commission, the irresponsible activities of such light-hearted physicians might to a certain extent be neutralized in the future if a physician were to be allocated special duties with regard to the police of Stockholm. In *Svenska Läkartidningen* for Dec. 2, Dr. Dag Knutson puts the problem in its right perspective by outlining the conditions under which physicians act as the medical conscience of the community. With the introduction of compulsory sickness insurance in Sweden at the beginning of 1955, the responsibilities of the medical profession as guardian of the purse, as well as of the health of the nation, have grown constantly. Apart from the rare exception of the irresponsible few who take their duties too lightly in this respect, the bulk of the medical profession shoulder the task of drafting medical certificates conscientiously but with growing distaste.

SWITZERLAND

Diabetes.—Various clinical and experimental works have shown that degenerative lesions of the blood vessels are closely related to lipid metabolism. Most patients with diabetes mellitus seen at the University Clinic of Geneva had various complications. A study was made of the quantitative and qualitative modifications of their serum lipids by A. Vernet and his co-workers (*Diabetes* **3**:181, 1955). Three tests were used: Sandor's reticuloendothelial curve, the lipidogram, and cholesterol determination. They studied the serum of 105 diabetic patients taken from the 250 patients regularly observed. The patients selected for study had the following complications: diabetic retinopathy, albuminuria, other vascular complications, disturbed reticuloendothelial curve, arterial hypertension, hypercholesteremia, and disturbed lipidogram. None of the 21 patients with retinopathy, albuminuria, and vascular complications had severe diabetes, but their lipid tests often showed abnormal reactions. Five of the six Kimmelsteil-Wilson syndromes histologically confirmed were found in this group. The presence of a humoral syndrome comprising hypercholesteremia, a disturbed reticuloendothelial curve, and a beta-alpha lipoprotein ratio greater than 5:1 in a patient with retinopathy and albuminuria is diagnostic of a beginning Kimmelsteil-Wilson syndrome and consequently an unfavorable prognosis. The second group included patients with retinopathy and vascular complications with albuminuria (value not exceeding 1 gm. per liter). In these, the tests again showed abnormal reactions. The third group consisted of 34 patients with retinopathy unaccompanied by other degenerative lesions. Although the incidence of abnormal reactions was not proportional to the duration of the retinopathy, a certain parallelism existed between the type of reticuloendothelial curve and the progressiveness and severity of the ocular lesions. The fourth group consisted of 14 patients with coronary, cerebral, or peripheral arterial complications similar to those of the second group. The evidence obtained from groups 2 and 4 suggests that the presence of retinopathy is closely linked to a humoral syndrome of disordered lipid metabolism. The evidence from group 3 shows that, when the humoral disturbances are great, the proportion of progressive retinopathies is greater than when they are partially absent. Group 5 consisted of 25 patients with no vascular complications. In them, the lipid metabolism tests rarely revealed abnormal reactions. It is noteworthy that in group 4, consisting of patients with arterial complications without diabetic retinopathy, arterial hypertension preceded the appearance of the diabetes by an average of two years. Most of the patients in this group were arteriosclerotic and, therefore, usually hypertensive, and their diabetes developed late and was usually mild. The duration of hypertension compared with that of the diabetes has an important bearing on the prognosis. In patients with severe diabetes and progressive vascular complications, the diabetes is of much longer standing than the hypertension, which signifies that the hypertension is not essential and benign but rather a symptom of progressive nephropathy, with poor prognosis. Although all clinical forms of diabetes are not accompanied by a particular humoral syndrome, it is clear that disturbed serum lipid metabolism exists in patients with diabetes complicated by vascular lesions. The severity of the metabolic disturbances varies in proportion to the severity of the diabetes and the amount of nephropathy and retinopathy.

Neurosurgery.—At a meeting of Swiss neurosurgeons, Zander of Zurich stated that, in patients with acute post-traumatic subdural hematoma, exploratory trephination is necessary whenever the state of consciousness of a patient is altered in the hours following injury, even if unilateral mydriasis exists. In contrast to late subdural hematomas, which usually are localized in the convexity of the hemispheres and are, therefore, apparent on trephination performed several centimeters from the midline, acute subdural hematomas are usually localized in the inferior temporal region, as are epidural hematomas. It is, however, sometimes necessary to make an exploratory hole in the frontal and parietal regions or even in the posterior fossa. The trephination is not made in order to drain an effusion, as is done in chronic subdural hematomas. An osteoplastic trephination is necessary in acute subdural hematomas so that all clots may be evacuated and satisfactory hemostasis attained. Acute hematomas are usually caused by a focus of cerebral contusion and not by rupture of a vein that links the cerebral cortex to a large dural sinus. The case fatality rate is much greater than in patients with late subdural hematomas.

Richter discussed the advantages and disadvantages of serial angiography as compared with cerebral angiography as it is usually practiced; i. e., in three successive pictures. The advantage of serial angiography, which consists of 20 to 30 small films, is that a more complete picture of the cerebral circulation is gained. Radiologists are less exposed to dangerous radiations with this procedure. The disadvantages are that the procedure is more expensive and that the small films are not always easy to interpret. The method is of greater scientific than practical interest. A. Werner reported that he operated on two patients with cerebral cysticercosis. He used decompressive posterior trephination associated with supraoptic ventriculostomy for the prevention or cure of internal hydrocephalus. The cysticerci should be removed with the greatest care in order to avoid their breaking, because they contain an endotoxin that may cause a fatal dementia. G. Weber of Zurich said that it is difficult to make a diagnosis of tuberculous meningitis in patients who enter the hospital with a diagnosis of tumor or abscess. Antituberculous therapy should be instituted immediately in all cases of lymphocytic meningitis of uncertain cause without waiting for laboratory reports.

Aldosteronuria and Hyperkalemia.—A. Falbriard and his coworkers (*Schweiz. med. Wchnschr.* **85**:1218, 1955) studied the variations in aldosteronuria under the influences of potassium surcharge and renal and extrarenal loss of water and salt. They found that normal persons show increased urinary excretion of aldosterone under the influence of potassium surcharge, a

carboanhydrase-inhibiting diuretic, and the combination of these substances. The effect is due to compensating adrenal hyperfunction, caused by the hydrosaline loss, but potassium may also have a direct effect on aldosterone secretion. The influences of sodium loss and of water loss cannot be dissociated. Progressive urinary excretion of aldosterone also occurs in excessive sweating. This experiment was performed in order to cause a reduction of total liquid volume with moderate sodium retention due to hypotonicity of the sweat. The resultant hypernatremia reflects the dissociation of water and salt loss. In this situation, the reduction of extracellular volume would seem to be a primary factor in aldosterone hypersecretion. Another dissociation that was noted was that between urinary excretion of aldosterone and that of the 17-hydroxysteroids. The latter did not vary significantly under any of the different influences studied. However, the plasma content of 17-hydroxycorticosteroids became elevated during sweating produced by physical effort. Perhaps the endogenous secretion of corticotropin, associated with effort, plays a partial role in aldosterone hypersecretion; a preliminary experiment seems to indicate the possibility of a facultative dependence of aldosterone secretion in relation to corticotropin.

Thus, hyperaldosteronuria can occur in the normal person after renal or extrarenal loss of sodium and water. It explains the compensating hydrosaline retention. Since this hyperaldosteronuria is seen in the presence of variable amounts of urinary sodium, it seems that aldosterone secretion is connected less to the absolute quantity of eliminated sodium than to variations in hydromineral metabolism. Furthermore, progressive excretion of aldosterone was seen in two other patients after an abrupt decrease in the dietary sodium supply (from 270 to 160 mEq. per day). This effect corresponds to the phase in which renal sodium excretion is adapting itself to the variation in supply. Thus, aldosterone secretion appears to be important as an adaptation and conservation mechanism tending to maintain hydromineral balance.

UNITED KINGDOM

Long-Term Chemotherapy in Pulmonary Tuberculosis.—A series of 142 patients with pulmonary tuberculosis who had received chemotherapy for at least nine months, 63 of whom have been followed for at least one year following completion of treatment, has been studied at the Brompton Hospital by Clifford Hoyle and his co-workers (*Lancet* **2**:1310, 1955). The usual course of chemotherapy for the first 6 to 12 weeks was 1 gm. of streptomycin intramuscularly every day with either 16 to 20 gm. of aminosalicylic acid in four doses, or 100 mg. of isoniazid every 12 hours. When cavities closed or the sputum became negative, the 1 gm. of streptomycin was given only two or three times a week but aminosalicylic acid was given daily. The duration of treatment ranged from 9 to over 24 months, and many of the patients were back to work before chemotherapy was finally stopped. Of the entire series, 101 were treated solely by rest and chemotherapy, and the rest received some ancillary form of treatment, usually surgical. Results were assessed mainly by radiographic and bacteriological methods.

The radiographic findings remained unchanged in 13 (9%) throughout the period of treatment. All the others had improved: 18 for three months, 38 for six months, 49 for nine months, 20 for one year, and 4 for more than one year when last seen. In 64 of the 92 patients with cavitation, the cavities were cleared by chemotherapy alone. Before treatment the sputum was positive in 111 patients. The incidence of positive sputum after treatment was 26% after three months, 16% after six months, and 8% after nine months. The nine patients with positive sputum after nine months' treatment still had cavities. These had been more than 3.5 cm. in diameter before treatment. Tubercle bacilli resistant to streptomycin and aminosalicylic acid were found at some time in all nine patients from whose sputum tubercle bacilli were isolated after a year's treatment. Only three of these patients produced organisms resistant to isoniazid, and these were the only three patients who had received isoniazid for longer than the initial three months' treatment. With one exception, none of the patients in whom resistant tubercle bacilli were discovered have so far deteriorated from the state of maximal improvement earlier achieved, and six of them have had chemotherapy for more than three years. Among the toxic effects, nausea was common with aminosalicylic acid therapy. Three patients became deaf with use of dihydrostreptomycin—two permanently.

The follow-up shows that four patients died: one from disseminated lupus erythematosus, which was present before chemotherapy was instituted; one after an operation for acute intestinal obstruction; and two from tuberculosis (one after thoracoplasty). Of the remaining 138, 126 are leading their ordinary lives with full activity and 10 others are bothered to some extent by breathlessness. Up to June, 1955, 78 patients had been observed for six months or longer (63 for more than a year) after completion of treatment. Apart from the two who relapsed, all maintained their progress and were at work, as at the end of treatment.

Copper in Food.—The Food Standards Committee of the Ministry of Agriculture, Fisheries, and Food, in a report on the permissible limits of the copper content of food, notes that in the light of present knowledge it is not possible to assess the risk to health that may arise from the consumption of foods with an unusually high copper content. The presence of harmless amounts of copper, however, can render many foods and beverages unpalatable. From the public health standpoint, copper is in a different category from arsenic and lead, and the committee believes that the consumer will be adequately protected if limits consistent with good commercial practice are observed. The report confirms the general limits before recommended, i. e., 2 parts per million of copper for ready-to-drink beverages and 20 parts per million for other foods, and the statutory limits previously recommended for edible gelatin (30 parts per million) and tomato catchup (50 parts per million of the dried total solids) but adds certain further limits. These include 7 parts per million for nonalcoholic drinks prepared from cider and concentrated soft drinks, 20 parts per million for concentrates used in the manufacture of soft drinks, 60 parts per million (of dry matter) for yeast and yeast products, and 300 parts per million for solid pectin.

In the case of tea, a limit of 150 parts per million is recommended. This takes account of reports received from the Tea Research Institute of Ceylon on the treatment of blister blight, a disease that seriously affects the shrubs from which tea leaves are obtained. Control measures involve the use of copper fungicides, and under certain weather conditions it is impossible to avoid a high degree of contamination. The committee understands that it may be possible to work to a lower limit when further experience with methods of control has been gained and considers that the limit of 150 parts per million should be regarded as provisional and reviewed periodically. In the meantime the committee believes that no exception need be taken to the importation of tea containing not more than 150 parts per million of copper. Only a fraction of the copper in the leaf is soluble, and, in view of the proportion that the weight of the infusion bears to the weight of the leaf, the copper content of the infusion would not normally exceed the limit of 2 parts per million recommended for ready-to-drink beverages. The committee concludes that, although there may be occasions, as with edible gelatin and tomato catchup, to prescribe statutory limits for a few foods that are particularly liable to copper contamination, in the absence of any new development it is unnecessary to give statutory effect to the limits now recommended.

Sleep Behavior in the Aged.—The sleep behavior of the aged has been investigated by N. R. Cowan (*Health Bulletin* **14**:7, 1956) in a series of 313 patients aged 70 years and over, who were seen at a health center for older people in Scotland. Good sleep was noted in 182 (58%) of the patients. Advancing years had no detrimental effect on the sleep of the patients. Marital status, on the other hand, made a significant difference: 24 (77%) of the single patients, 79 (64%) of the married patients, 42 (55%) of the widowers, and 37 (45%) of the widows slept well, and 5 (16%) of the single patients and 26 (32%) of the widows slept poorly. The state of health of a patient was reflected in the quality of his sleep. Of 97 patients who were

contented with life and had no physical complaints, 91 (94%) slept well, compared with only 9 (15%) of the 58 who were discontented with their lives and had physical complaints. Sleep during the day had no significant effect on the quality of sleep at night. Of the 121 patients who habitually slept during the day, sleep at night was good in 71 (59%), fair in 21 (17%), and bad in 29 (24%). The comparative figures for those who did not sleep during the day were 111 (58%), 37 (19%), and 44 (23%). Among the 186 patients who took longer than half an hour to fall asleep, the commonest cause was undiminished or increased activity of the mind on retiring. The next most common cause was reading in bed prior to falling asleep. In 55 patients there was no specific cause, and in 14 it was attributed to pain. Of the 58 patients who lived alone, 36 had difficulty in falling asleep and 17 of these attributed this to loneliness. Nocturnal micturition was an important cause of disturbed sleep in both men and women: 75% of the entire series had to get up three or more times during the night. Nocturnal cramps were the next most common cause of disturbed sleep. These occurred in 28% of the 70-74 age group, 29% of the 75-79 age group, 30% of the 80-84 age group, and 25% of those aged 85 and over. The sexes were equally affected, except that none of the women over 85 had night cramps.

Emergency Bed Service.—A report on the London Emergency Bed Service was presented to the King Edward's Hospital Fund for London by Dr. G. F. Abercrombie. The service was initiated by the King Edward's Hospital Fund in 1938 to help general practitioners in admitting patients in urgent cases to a hospital. All that the practitioner had to do was to give the service the details by telephone and the service then made the necessary arrangements. The scheme was so successful that by 1948 the service was dealing with about 13,000 cases a year. When the National Health Service came into being in that year, this number was immediately doubled, and the service now deals with 65,000 applications a year. On an average, 27 minutes are required for a successful admission, from the general practitioner's initial call to the service's request for an ambulance. The busiest day ever recorded was Dec. 2, 1952, at the height of the great smog, when 564 requests for admission were received. In summer the weekly total falls below 800, and 97% of these are admitted. In winter the weekly total is between 1,600 and 2,400, and the admission rate tends to fall. The service boasts that every patient represented as being in urgent need of treatment that can be obtained only in a hospital is found a bed. For dealing with crises, a warning system has been evolved. If the percentage of success falls below 85, a white warning is sent to all hospitals. This precautionary signal means that the service is hard pressed and may be in serious difficulties in a day or two. If the percentage falls below 80, the warning is yellow, and, if below 75, red. These are urgent calls for help and mean that the resources of the service are being exhausted. On receipt of these warnings, hospitals take their prearranged action to provide more beds, and as a result of their cooperation the percentage of success has not fallen below 80 since the influenza epidemic of February, 1953. A further function of the service is that its daily records serve the Ministry of Health as a sensitive index of the rise and fall of sickness among the people of London.

Prescribing Drug Samples.—Under the National Health Service, patients have to pay 14 cents toward the cost of each prescription. Normally, only a pharmacist is allowed to dispense prescriptions under the health service, and he is responsible for collecting the prescription charge from the patient. In rural areas, however, if there is no reasonably accessible pharmacist, physicians do their own dispensing and they are then responsible for collecting the prescription charge. A case has recently been reported in which such a country practitioner was charged with failing to collect this charge from his patients. The defense was that he used free samples from drug houses to stock his dispensary and he did not feel justified in charging his patients for them. On his rounds he always took with him a large supply of the "literally hundreds" of samples he received. He found this a satisfactory method of dispensing, and it saved much time. He also kept a small stock of ordinary medicines in his dispensary, but, when he came to collect the prescription charge on these, his patients would present him with a pound note, for which he had no change. He then found it difficult to collect the charge, but he avowed that he had remitted all the charges he had collected. The executive council before which he appeared decided that $28 was a reasonably accurate estimate of the amount involved and that this should be withheld from the physician's remuneration.

What Is a Drug?—If a practitioner prescribes for one of his health service patients a preparation that is not recognized as a drug by the Ministry of Health, he is liable to a surcharge equivalent to the cost of the preparation he has prescribed. This problem most often arises in the case of preparations that lie in that ill-defined range between foods and drugs. It also arises in connection with barrier creams, and an interesting demonstration of the difficulties facing the physician is provided in *Prescribers' Notes*. Details are given of four cases recently determined by referees. Patients 1 and 2 both suffered from chronic eczema of the hands. The view was taken that, since the cream was given to relieve the patients from having to wear rubber gloves or from having to pay someone else to do the washing, it was not a drug. Patient 3 had contact dermatitis, and the barrier cream was prescribed to prevent recurrence. It was decided that the action intended here was mechanical rather than medicinal and that it was therefore not a drug. Patient 4 suffered from a permanent cecostomy that caused recurrent excoriation of the skin around the opening. The referee considered that there was some justification for ordering the barrier cream and considered it to have been prescribed as a drug in this case. The optimistic official view expressed is that these decisions may help to give guidance.

Poliomyelitis and Smallpox Vaccination.—Evidence suggesting that poliomyelitis seldom attacks children who have been vaccinated against smallpox during the previous few years is advanced by D. P. McIver (*Lancet* **1**:226, 1956). Between 1946 and 1954, of a series of 11,842 children, 53% were vaccinated against smallpox. In this period 21 cases of paralytic poliomyelitis occurred in unvaccinated children under 5 years of age and only 4 among the vaccinated. This contrast is even more striking among children under 3½ years of age; 18 cases of paralytic poliomyelitis (with three deaths) occurred among the unvaccinated children and only one case (nonfatal) among the vaccinated children. This inverse relationship between smallpox vaccination and poliomyelitis was not found in children 5 to 15 years of age; 18 among the vaccinated and 16 among the unvaccinated contracted poliomyelitis. In the same period 34 persons over 15 years of age contracted paralytic poliomyelitis; none of them had been vaccinated against smallpox within recent years.

Cadmium Poisoning and Byssinosis.—The Ministry of Pensions and National Insurance has announced that people whose occupations involve exposure to cadmium fumes will now be insured under the Industrial Injuries Scheme against chronic as well as acute cadmium poisoning. Previously benefits could be claimed only for acute cadmium poisoning. It is also announced that people suffering from byssinosis will find it easier to qualify for industrial disability benefits. Previously benefits for byssinosis could be claimed only by people who had been employed for at least 20 years in the cotton industry, provided the disability from byssinosis was assessed at 50% or more. Under the new regulations the period of qualifying employment is reduced to 10 years, and the condition that benefits cannot be paid unless the disability is assessed at 50% or more has been removed.

Orally Given Poliomyelitis Vaccine.—An orally given vaccine against poliomyelitis prepared by Dr. Koprowski of Lederle Laboratories, Pearl River, N. Y., is being tested at Queen's University, Belfast, by Prof. G. W. A. Dick. The vaccine contains attenuated types 1 and 2 strains only, as an attenuated type 3 strain is not yet available. Work on the production of such a strain is being carried out at Belfast. The aim of the tests that are being carried out on volunteers in Professor Dick's department is to investigate the antigenic power of the vaccine.

CORRESPONDENCE

DRUGS FOR ARTHRITIS

To the Editor:—In Dr. Boland's article, "Prednisone and Prednisolone Therapy in Rheumatoid Arthritis," appearing in the Feb. 25, 1956, issue of THE JOURNAL, page 613, a comparison of these two medicaments with hydrocortisone is made. I wish only to comment on the ulcerogenic properties of these medicaments, which the author found to be increased by the use of prednisone and prednisolone. My experience with the latter two medicaments is based on the treatment of ulcerative colitis, regional enteritis, and liver disease. I have not found an alarming incidence of peptic ulcer or digestive complaints in my patients, most of whom have had an upper gastrointestinal x-ray study prior to administration of therapy. Perhaps the nature of the patients treated by Dr. Boland and the procedure of study should be further analyzed. In common with most studies printed on the ulcerogenic properties of steroid therapy, control gastrointestinal x-ray studies were not made before treatment. It seems to me that this is important because of the acknowledged, but not too accurate, sizeable incidence of peptic ulcers in the general population. For instance, in "Peptic Ulcer," (Philadelphia, W. B. Saunders Company, 1951, p. 192) it is roughly estimated that 10% or more of the population have an ulcer. Various autopsy series are quoted, ranging from 2.6 to 16.7%. A recent comprehensive study by Tomenius (*Acta med. scandinav.* **152:** 391-411, 1955) of the population of Stockholm, Sweden, resulted in a 6.5% incidence of ulcer in males and 2.0% in females. As for rheumatoid arthritis, Bauer (Proceedings of the Conference on the Effects of Cortisone, Dec. 10, 1951, Rahway, N. J., Merck & Company, Inc., 1952) reported a 4.5% incidence of peptic ulcer in patients prior to steroid therapy. Any writer claiming a significant increase in the incidence of peptic ulcer due to a medicament must keep these figures in mind.

Dr. Boland divided his patients into three groups. In group 1, consisting of 32 rheumatoid patients who had not been previously treated with any steroids, only 5 patients had gastrointestinal symptoms and, of these, only 2 had x-ray evidence of duodenal ulcer. This is an incidence of ulcer of 6.3%, which would not differ from that of hydrocortisone. Certainly this is not an incidence to cause alarm. Group 2 consisted of 39 patients satisfactorily controlled with hydrocortisone, who were transferred to the metisteroids (prednisone and prednisolone). In this group, five patients had gastrointestinal symptoms, but in none was there x-ray proof of peptic ulcer. Therefore, in groups 1 and 2, consisting of 71 patients, the incidence of proved ulcer was less than 3%, a rather insignificant figure. Group 3 was comprised of 70 patients who had received hydrocortisone for an average of 19 months but whose rheumatoid arthritis was not satisfactorily controlled. These patients were then given metisteroids in larger dosage than given the patients in groups 1 and 2, and, according to Dr. Boland's data, 26, or 37%, of these had symptoms but only 7, or 10%, had ulcers proved by x-ray. Of these seven patients with proved ulcers, three had sudden gross hemorrhage. Actually, it was on the basis of his experience with group 3 patients that Dr. Boland concluded that there is a greater propensity for digestive complaints with the metisteroids. It is quite apparent that the group 3 patients had the most severe cases of arthritis, and with the greatest stresses and strains (economic, social, and mental, as well as physical) they would probably be more apt to have peptic ulcer than patients in the other two groups. Furthermore, group 3 patients had been on long-term hydrocortisone therapy prior to administration of the metisteroids and larger doses of all the steroids were administered than in the other two groups. In group 2, patients previously satisfactorily controlled by hydrocortisone, the change to metisteroids, in lesser dosage than given to group 3 patients, resulted in no ulcers diagnosed by x-ray. Actually, when one compares groups 1 and 2 with group 3 (71 and 70 patients respectively), there is an incidence of two ulcers proved by x-ray in 71 patients of groups 1 and 2 (2.8%) contrasted with seven proved cases of ulcers in group 3 (10%) patients. The incidence of peptic ulcer in groups 1 and 2 is an insignificant figure that would be hard to attribute to any therapy, since the known incidence of ulcer in the general population is higher than this. The higher incidence of ulcer in the group 3 patients indicates the unique nature of this group. Dr. Boland's provocative article and findings indicate the need for further controlled studies on the ulcerogenic properties of the steroids, of whatever variety, since the evidence to date does not appear to show that any specific type of steroid therapy has a greater ulcerogenic propensity than another type.

IRVING B. BRICK, M.D.
Department of Medicine
Georgetown University Medical Center
Georgetown University Hospital
Washington 7, D. C.

TRANSFUSION SERVICE IN ATOMIC BOMBARDMENT AREAS

To the Editor:—The amount of blood needed to support the medical service that is charged with care of casualties in an area bombarded with nuclear weapons would seem to be a proper subject for guesswork, but, still, it is susceptible to some analysis if we know what sort of medical service is possible within present knowledge and with present tools. Perhaps the most important thing to recognize in the situation is that we cannot project our requirements for blood or anything else from a basis of experience in conventional warfare. The combat zone in modern warfare is a highly complex and well-organized area occupied by a smoothly functioning organism, the combat army. The medical service of this army is almost always "on top of its environment," retrieving, evacuating, and caring for its wounded in an effective fashion. Atomic detonation over an inhabited area instantly demolishes the social organism and, at the same time, produces a fantastic number of wounded. There is no well-controlled stream of casualties, but, instead, there is one sudden avalanche and then, presumably, no more. Any medical service, however well organized, would be snowed under. Reaction time may be short, and organization of some degree of effectiveness may be quickly restored, but while this takes place time is lost and wounds grow worse. How does this situation modify the transfusion service and the requirement for whole blood and blood substitutes?

During World War II and the Korean war the amount of whole blood used in the combat zone increased continually. Early in World War II the first transfusion service was established by the British in North Africa. During that campaign they used 0.2 units of whole blood per man wounded in action. This figure, of course, represents the rate of use. It does not signify that every man wounded in action was given whole blood nor is it the average only of those given transfusion. The figure is referred to as a "use factor." During combat on the mainland of Europe later in the war the use factor increased to 0.5 units of whole blood per man wounded in action, and during the Korean war it grew to 0.9 units. The Korean figure reflects an exceptional situation. That war, during its last year, was static, and the delivery of supplies, including blood, was relatively uncomplicated. The flow of casualties was generally light, so that it was possible to give each casualty intensely individualized treatment. Many poor-risk casualties, who might otherwise have died, were salvaged by (1) rapid evacuation often by helicopters carrying a single man wounded in action, (2) vigorous resuscitative measures administered by smooth-working teams, and (3) prolonged and often intricate surgery. In the Korean situation whole blood was available in unstinted quantity. It was available not only in the surgical hospitals but also in the division areas and even, under some circumstances, in battalion

aid stations. During resuscitation and surgery blood was used in preference to other available materials, such as plasma, albumin, and dextran. Blood was often used when one of the others might have sufficed. At the surgical hospitals blood was used almost to the exclusion of the others. Even under these conditions approximately 80% of the men wounded in action received no blood transfusion at all during their treatment in the combat zone. The 20% who had transfusions were, of course, the most severely wounded. It seems evident from World War I experience—when there were no blood transfusions and less than 8% of the men wounded in action died—that many of the seriously wounded in the 20% group with transfusions could have survived without transfusion. We may deduce that the use factor for whole blood, based on the Korean experience, reflects a situation remarkably like that claimed by G. B. Shaw as the reason for the success of matrimony as an institution. In Korea there was an ample provision of blood and ample opportunity to use it. The use factor for blood, 0.9 units per man wounded in action, probably represents a ceiling for whole blood that we are not apt to exceed, since the circumstances of war are not likely to be more favorable for patient care than they were in 1953. Because blood was used preferentially, the use factor for all resuscitative fluids, such as blood, plasma, or synthetics, would seem to be not much greater than 0.9 units per man wounded in action. Therefore, in attempting to decide how much blood or blood substitute may be needed for a disaster of any sort, a factor of 1.0 units per casualty may be set as an outside figure, with fair assurance that the requirement will not exceed that figure. Under some conditions, notably atomic bombardment, such a factor would be excessive.

The requirements for whole blood in case of atomic warfare will be considerably modified by circumstances. Tens, or even hundreds, of thousands of casualties will appear suddenly. Then few more, if any, will occur in that immediate area. Optimal conditions for provision and use of blood will not be present, and careful, individualized treatment of poor-risk casualties will not be possible. Those who might be salvaged by rapid evacuation, immediate transfusion, and first-rate surgery will die before they can be recovered and hospitalized. The demand for blood to meet the immediate requirements after injury—during the six "golden" hours—will be almost nil. Even if 100,000 units of blood were miraculously made available instantly, the blood could not be used effectively because the thousands of severely wounded could not be recovered, sorted, and individualized in time. Good-risk and fair-risk casualties would be given priority, and most of them could get by without transfusions. How much blood can be made available during the first hours after an atomic bombardment? The New York State Civil Defense Commission has developed tables of organization for blood bank teams. These teams would take blood from donors, process the blood—type, tag, and titer it, if it is universal donor blood—and prepare it for shipment. Such teams, working six-hour shifts, require about one man hour per unit of blood. In emergency, a team of 40 men working a 12-hour shift could provide 500 to 600 units of blood. Not many of the 1,500 blood banks in the United States are staffed, equipped, and indoctrinated to carry out taking and processing of blood on such a scale. If they were, they could accumulate 750,000 units of whole blood the first day. The actual amount that could be counted on today, with blood banks set up as they are, is estimated to be about 13,000 units per hour. This amount, though enormous, seems relatively small when compared with the requirement visualized in contemporary plans. "Operation Alert 1955" was a study of the damage that might be expected from an enemy attack on the United States. The basis for the study was to imagine the simultaneous bombing of 49 American cities that might reasonably be regarded as primary targets. The number of casualties was estimated to be 8 million. With the currently accepted "planning factor" of the Blood and Blood Derivatives Program for Civil Defense, this number of casualties would require, during the first three days, 5 million units of whole blood and an equal number of units of plasma or plasma expanders. The same amount would be required during the subsequent three weeks. The logistical situation that would prevail following atomic bombardment of United States cities is another factor that should be permitted to modify the plans for medical support. Harsh as it seems, experience shows that medical supplies are given low priority for transportation, when the means of transportation are squeezed by the requirements of war. First priorities are given to food, fuel, and ammunition. In such competition, the movement of medical supplies, however urgently needed, cannot be counted on. It seems probable that most, if not all, of the blood provided in support of the surgical teams would have to be locally procured at or near the hospitals where the casualties are cared for.

With these three considerations in mind—the amount of blood urgently needed, the amount that could be obtained, and the problem of transporting medical supplies—it seems appropriate to examine the Blood and Blood Derivatives Program for Civil Defense. The "TM-11-5 Blood and Blood Derivatives Program" bulletin (Federal Civil Defense Administration, 1953, pp. 1-2) states:

"As a general guide for planning, an average of one unit (500 cc.) of blood, plasma, or plasma expanders per casualty surviving after 24 hours, would be needed each week for the first three weeks. This is based partly on careful study of the military experience with battle casualties during World War II and partly on the data from Japanese casualties at Hiroshima and Nagasaki. Thus, for every 1,000 casualties, 3,000 units of blood, plasma, or plasma expanders would be required. About one-half of this amount (1,500 units) should be whole blood. This is based, to a large extent, on the necessity for using plasma and plasma expanders during the early postattack period when blood is not yet adequately available, rather than on ideal clinical requirements. This takes into consideration the fact that about one-third of the casualties will be walking wounded with relatively minor injuries, one-third moderately injured requiring short hospital care, and only one-third will have a serious degree of injury requiring extensive hospital care. Almost all of the latter group and a portion of the moderately injured group, including those exposed to radiation, will require one or more transfusions. Therefore, the 3,000 units will be given to about 400 to 500 casualties (40-50 per cent) surviving after 24 hours. This estimate provides an average of about six units per casualty requiring transfusion. The peak requirements will occur during the first 72 hours and again after the tenth to twelfth day for treatment of radiation sickness.

"In the hypothetical example employed in *Health Services and Special Weapons Defense* a single atomic bomb could, in daylight and with adequate air-raid warning and civil defense preparedness, result in 60,000 casualties in a typical American city. Approximately two-thirds of these casualties, or 40,000, would survive after 24 hours. This would require an estimated total of 120,000 units—60,000 units of whole blood and 60,000 units of plasma and plasma expanders—for the care of approximately 13,000 severely injured, and 3,000 to 7,000 of the moderately injured. These figures are used here for purposes of easy reference to other related data in the cited reference. However, recent developments indicate casualties could be considerably higher, possibly as high as 100,000 to 150,000, from a single burst."

This plan appears to require a maximum if not a superfluous amount of blood, plasma, and plasma expanders. If so, it may be criticized on two points: It is based upon an unrealistic concept of the type of medical and surgical treatment that would be possible following an atomic detonation, and it would necessitate the stockpiling of an excessive amount of supplies and equipment. A reevaluation of this problem, especially in view of the greater destructive potential of new weapons, might indicate that the amount of blood, plasma, and plasma expanders that would actually be used might be considerably less than 5% of the requirement presently set forth by the Blood and Blood Derivatives Program for Civil Defense.

LIEUT. COL. WILLIAM H. CROSBY, M.C.
Chief, Department of Hematology
Walter Reed Army Institute of Research
Walter Reed Army Medical Center
Washington 12, D. C.

LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Malpractice: Statute of Limitations.—The plaintiff filed a malpractice suit against the city of Miami for injuries sustained in a city-operated hospital as the result of an overdose of x-ray therapy. From a judgment for the plaintiff, the city appealed to the Supreme Court of Florida.

The plaintiff, while a paying patient at the Jackson Memorial Hospital, operated by the city of Miami, received an overdose of x-ray therapy, which was being used for the removal of verruca plantaris from her left heel. It was admitted that the cause of her injury was the negligence of the defendant's employees. The plaintiff sustained the injury in 1944. She became aware of the injury in 1949, when the first symptoms became visible, and she filed suit in 1950. The defendant contended, among other things, that the statute of limitations had run its course because of the time lapse.

The court reasoned that the statute should not start to run until there has been notice of an invasion of the legal right of the plaintiff or until the plaintiff has knowledge of his right to a cause of action. In many cases the injured party has no notice of the invasion of his legal rights until the injury materializes, and a contrary holding would deprive him of his remedy. Since the plaintiff had no notice of the injury until 1949, even though the negligence occured in 1944, an action brought in 1950 is not barred by the statute of limitations. However, said the court, if the plaintiff had known of the injury in 1944 but had not known of the consequences until 1949, an action brought in 1950 would have been barred by the statute.

The Supreme Court therefore affirmed the judgment for the plaintiff. *City of Miami v. Brooks, 70 So. (2d) 306 (Fla., 1954).*

Medical Practice Acts: Revocation of License for Conviction of a Crime.—The petitioner, a physician, had his license to practice medicine revoked pursuant to the provisions of the law of New York. The case was appealed through the state courts (*111 N.E. (2d) 222; J. A. M. A.* **157**:1436 [April 16] 1955) and was eventually appealed to the Supreme Court of the United States.

In 1946 the petitioner was subpoenaed by the House Committee on Un-American Activities and ordered to produce all the records of the Joint Anti-Fascist Refugee Committee of which he was then national chairman and member of the executive board. On the advice of his attorney the petitioner refused to produce these records, and he was eventually tried and convicted of violating the pertinent federal statute. After this conviction, a complaint was filed against the petitioner under the New York Education Law, which authorizes suspension of a physician's license for conviction of a crime either within or without the state of New York.

The Supreme Court held that the suspension did not violate constitutional due process, because the practice of medicine is not a constitutionally guaranteed right but a privilege that vitally affects the health and welfare of the state and that, therefore, may be limited by the state under its police power. The Court pointed out that the facts of the petitioner's case fell squarely within the meaning of the statute; that, although the statute might be "stringent and harsh," it was clear and unambiguous; that the petitioner had in fact been convicted of a crime; and that the petitioner had enjoyed due process in having his contentions heard, both by the board and by the courts.

Accordingly, the Supreme Court held that the statute was constitutional and that the revocation of the petitioner's license to practice medicine should be affirmed. *Barsky v. Board of Regents of University of State of New York, 74 S. Ct. 650 (1954).*

Malpractice: Abandonment of Patient.—The plaintiffs, husband and wife, sued the defendant physician for damages for allegedly having failed to attend and treat the wife during her confinement. From a verdict in favor of the defendant, the plaintiffs appealed to the Supreme Court of Missouri.

Mrs. Small became pregnant, and the defendant doctor was engaged to look after her during her confinement. The defendant saw Mrs. Small in his office from time to time prior to Jan. 9, 1950, but, on that day, she discovered a vaginal discharge and noted an increase of pains in her abdomen and legs from which she had been suffering for a little over a month. On Jan. 11, she telephoned the defendant, and he advised her to get more rest, suggesting that she take Amytal sodium as a sedative. Two nights later Mr. Small telephoned the defendant around midnight, but the doctor advised him that his wife did not need a physician's care just then. Within three hours, however, she gave birth to a child. Mr. Small again contacted the defendant, and Mrs. Small was immediately taken to the hospital, where the defendant removed the placenta. The baby, however, died. The plaintiffs contended that the physician was guilty of abandoning the patient.

At the trial, conflicting testimony was given concerning the midnight telephone conversation on the night of the birth. Mr. Small testified that he had told the defendant that his wife was in extreme pain, that she was screaming, and that she was lying on the living room floor but that the defendant had refused to come to their home. The defendant testified that Mr. Small had said that his wife was uncomfortable and could not sleep but that no mention had been made of her screaming and lying on the living room floor. In response to a specific question, Mr. Small had told the defendant that his wife's pains were not intermittent. An expert medical witness for the plaintiff gave his opinion that, if the facts brought out by the plaintiff's evidence were true, the patient had not received adequate care. On the other hand, an expert testified for the defendant that, if a pregnant woman had a little flow of blood, an ordinarily careful physician would prescribe rest and that, if he were told that a pregnant woman was not having intermittent pains, he would say she was not in labor and would leave her at home.

The Court held that the issue was properly one of fact to be decided by the jury and that the jury's verdict was amply supported by the evidence. It was within the province of the jury alone to pass on the credibility of conflicting witnesses.

Accordingly, the judgment in favor of the defendant physician was affirmed. *Small v. Wegner, 267 S.W. (2d) (Mo., 1954).*

Workmen's Compensation Acts: Employee's Refusal to Undergo Surgery.—The plaintiff filed a petition for a compensation award against his employer. From an adverse judgment, the defendant appealed to the court of appeals of Louisiana.

The plaintiff worked as a truck driver and log loader. While stacking logs, his left leg became jammed between two logs and he fell sideways, twisting and injuring his left knee. The injuries consisted of a torn semilunar cartilage, or meniscus medialis, and a torn medial tibial collateral ligament of the knee joint. By the time of the trial, the torn end of the ligament had calcified for approximately ½ in. (Pellegrini-Stieda disease). The defendant's insurance carrier offered to have the plaintiff operated on to cure this condition, but the plaintiff refused to accept the offer. Accordingly, the defendant requested the court to order the plaintiff either to submit to the operation or to forfeit his right to collect further payments for his disability.

As a general rule, said the court of appeals, courts are reluctant to require injured litigants to submit to operations in order to collect workman's compensation. An employee, however, has no right to destroy his usefulness by wilful neglect or refusal of simple and harmless treatment as a means of recovery in order to obtain compensation. The court proceeded to examine extensively the expert medical testimony in the case and concluded that the requested operation, a removal of the meniscus medialis, would neither be unduly painful nor involve any serious risk and that it offered a high probability of nearly complete recovery. The court further found that the plaintiff had no good reason for refusing to submit to the operation. Specifically, the court found that a general fear of operations and anesthetics was not a reasonable ground for refusal. In view of this and of the slight risk involved, the court therefore held that the plaintiff's refusal to submit to the operation was unreasonable and arbitrary.

Accordingly, the judgment in favor of the plaintiff was affirmed but modified to the effect that, if the plaintiff refused to submit to the offered operation within 60 days, the defendant should have the right to discontinue making compensation payments. *French v. Employers Mutual Liability Insurance Company of Wisconsin, 70 So. (2d) 179 (La., 1954).*

MISCELLANY

THE DOCTOR LOOKS AT THE CANCER PROGRAM

This article has been prepared by the National Opinion Research Center for THE JOURNAL.

The present campaign theme of the American Cancer Society is "Fight Cancer with a Checkup and a Check," and, if the society's efforts are as successful as they would like, doctors all over the United States will face an unprecedented demand on the part of the public for "a complete medical checkup"—with emphasis on cancer.

How does the average family physician react to the public education activities of the American Cancer Society and its affiliated local committees? Does he himself really believe in the importance of frequent tests to facilitate early diagnosis of the disease? Does he believe that mass education campaigns have led to a greater and more knowing use of medical facilities? Or does he feel, as some have charged, that the cancer campaigns have been built on an unhealthy basis of fear and that the further expansion of efforts to detect this disease merely divert time and money from more urgently needed things?

Preliminary General Studies

Answers to such questions are now available, in the form of opinions of the doctors themselves, freely expressed when they were questioned by trained interviewers of the National Opinion Research Center last summer. These questions asked of doctors about cancer education were a part of a broad program of research in health that the National Opinion Research Center has been carrying out during the last several years under a series of grants from the Health Information Foundation. The first study under this program was a national survey of family medical costs in 1953-1954, which provided, for the first time in 20 years, a comprehensive picture of the medical expenses actually incurred by American families and the means by which these expenses were met.[1]

An important result of the first study was the finding that families of the same general age and income status nevertheless differed widely in the amount and kinds of medical care they received and sought. In consequence, the National Opinion Research Center's 1955-1956 research under this program has been designed to illuminate the subjective factors, such as knowledge, beliefs, attitudes, and satisfactions with past experience that affect people's health practices and use of medical facilities, and, incidentally, to turn up facts about public relations problems of doctors, nurses, druggists, private insurance groups, voluntary health agencies, and others who provide or are concerned with medical care in the United States. The research has had the interest and support of the professional societies and agencies concerned, including the American Medical Association.

During the summer of 1955, lengthy and detailed interviews were conducted with about 2,400 individuals, who represented a scientifically selected cross section of the total adult population. In the course of these interviews, the respondents were asked to name their regular doctor or, if they had none, the doctor they would most likely call in case of need. From the list of those mentioned, a random selection was made of names of 500 doctors, and these physicians were interviewed using a separate questionnaire that focused on the doctor's professional problems, his satisfactions and dissatisfactions, his views about the general public's attitudes and behavior with respect to health, and his relations with other professional groups with which he comes in contact. It will be noted that the doctors interviewed were not selected from lists or directories. Rather, each one had been named by at least one of the sample families as the family physician or regular doctor. This sample of approximately 500 doctors was thus designed to represent, not the medical profession as a whole, with its various types of specialist, but the thousands of personal physicians to whom people turn first for medical care. The sample was restricted to physicians who serve as family doctors because of the intimate contact such physicians have with the health practices of the general public. The day-to-day experience of these practitioners puts them in an excellent position to evaluate the effectiveness and general consequences of mass programs of health education and makes their opinions of the educational goals and methods crucial determinants of the programs' success.

General Approval of Program

Since the voluntary health agencies play a major role in the mass education program, some questions were included concerning doctors' opinions of these agencies, and, through a small supplementary grant from the American Cancer Society, it was possible to enlarge this section of the interview schedule and to probe more thoroughly into doctors' views toward the cancer program in particular. The results show that, while the average family physician has reservations about some aspects of the cancer program, he is generally sympathetic with both the content and the method of its educational activities and that his over-all attitude may be described as one of strong acceptance.

A brief summary of the tabulated answers shows, for example, that the average physician strongly endorses the American Cancer Society's injunction to "go straight to your doctor at the first sign" of any of the "seven danger signals" of cancer. He is convinced that more people actually do come to his office at earlier stages of illness than was the case 10 years ago, he spontaneously mentions that he has noticed this particularly in the case of cancer, and he credits the voluntary health agencies for a great deal of this result. He believes that all adults should get a general physical checkup every year, even if they feel fine, though he himself seldom makes any point of recommending this to his patients. He subscribes to the cancer program's urging of monthly breast self-examination and semiannual pelvic examinations for all women over 35 years of age, but he is inclined to draw the line at semiannual chest x-ray examinations for all men over 45, in spite of the efforts of the society to encourage this practice.

With regard to public education, he thinks it very important for the public to be better informed than it is about health and medical matters, and he is inclined to blame the public itself, rather than any particular groups, for the ignorance and misconceptions that exist. Perhaps surprisingly, he gives a large measure of credit for whatever correct knowlege the public does possess to magazines, television, and newspapers, though he frequently criticizes these mediums for spreading misinformation. He finds it easy to name constructive purposes served by the mass education campaigns of the voluntary health agencies and somewhat more difficult to think of any harm they have done. He seems generally content with the programs as now set up but is more likely to think of additional things they should do than of any present activities that he feels should be curtailed or changed.

This composite picture catches only the broad outlines of the doctors' views about the American Cancer Society educational program. It does show that, by and large, the program commands the sympathy and support of the "grass roots" of the medical profession. But in some respects the composite picture may be misleading. For one thing, it fails to take account of the sometimes sizable minorities of doctors who disagree with some of the society's recommendations or who criticize the manner in which the society's campaigns are conducted.

Minority Criticisms

A closer look at the survey findings reveals some interesting facts about doctors' opinions on these matters. (A report based on preliminary tabulations of doctors' answers to these questions was presented to the American Cancer Society in November, 1954. A detailed analysis of the final figures, insofar as they bear on the general problem of public health education, will appear in a forthcoming volume by the National Opinion

Research Center, reporting on the over-all results of this program of research.) For example, although practically all the physicians interviewed urge immediate consultation with a doctor in the presence of an actual complaint that might signify cancer, the proportion who support the idea of preventive checkups is significantly lower. Thus, percentages ranging from 92% to 100%—depending on what the complaint is—say that a person "should see a doctor right away" about such symptoms as a sore that doesn't seem to heal, an unusual bleeding or discharge, or a persistent cough. The only "danger signal" of cancer that a significant number of doctors felt did not warrant an immediate visit to a doctor was "any change in normal bowel habits," which was paraphrased in the interview as "diarrhea or constipation for a week." One doctor in four felt this should be taken care of at home "unless it kept up or got worse."

But the virtual unanimity of doctors as to the need for prompt treatment of these complaints falls off rather sharply when they are asked about preventive checkups in the absence of any complaint. About one doctor in 8 says flatly that such checkups are not worth the trouble if the patient generally feels well, while another one in 10 says they are useful only for persons past a certain age or with a particular medical history. Thus, as compared with the 92% to 100% who approve the "danger sign" approach, only 77% of the doctors unqualifiedly endorse the annual checkup for all. When it comes to the more specific preventive measures urged on the public by the society, the proportion of doctors who confirm their importance, in all but one instance, falls somewhat lower. Although 79% approve of the monthly breast self-examination, only 71% believe that semiannual pelvic examinations are necessary for all women over 35 years of age. And in the case of semiannual chest x-ray examinations for all men over 45, a clear majority of 58% does not approve.

The reasons offered by the disapproving doctors on these questions tend to restate the disbelief of this group in the importance of preventive checkups. In the case of the pelvic and chest x-ray examinations, the most frequent reasons are simply that such tests are not necessary and that they are not necessary so often unless the person has some complaint or there is some specific reason for the tests. More rarely it is explained that the incidence of the disease doesn't justify the time and expense, that such frequent tests tend to worry and upset the patient, or that the examinations are not always conclusive and may give a false sense of security. In the case of monthly self-examination of the breasts, on the other hand, disapproval is more often based on a belief that such a procedure leads to neurosis and morbid concern about cancer. It is sometimes held, too, that the average woman is not competent to make such an examination, that it can be done adequately only by a physician.

Endorsement and Practice of Periodic Examinations

The National Opinion Research Center interviews with the general public show that about 80% of adults—just as about 80% of doctors—endorse the principle of a general physical checkup every year "even if a person is feeling all right," but only 3 people out of 10 even claim to get such periodical checkups in actual practice. The doctors who were interviewed confirm that the annual checkup is seldom requested by their patients. A third of them say such a request is "unusual," and only 16% say that "many" of their adult patients come in for a general examination. If doctors themselves really believe in the importance of the annual checkup, the research indicates that the public's performance in this respect might be greatly improved by encouragement on the part of the physician. The great majority of adults already support the idea in theory, but they just do not get around to doing it. And at the present time, a majority of family doctors (55%) say they do not "make a point of recommending regular checkups." Thus, only 45% claim they suggest it to most of their patients.

Except for the semiannual chest x-ray examination for older men, large majorities of the doctors themselves say they approve of the tests and checkups urged on the public by the society. But do physicians feel that these campaigns are being somewhat overdone? Do they believe that too much information about cancer is being drummed into people by way of these mass campaigns, so that people's fears are being unduly raised and too much of doctors' time is being taken up with imaginary complaints? The answer is that some doctors do feel this way but the vast majority do not. On the contrary, the illness most frequently mentioned when doctors were asked, "What one or two things do you regard as most important for the public to learn about in the field of health and medical care?" was cancer (by 26% of all doctors). The illness mentioned next most frequently was named by only 15%.

Fear and the Program

Several questions in the interview schedule offered doctors an opportunity to criticize any overemphasis on fear they may have noticed in the cancer campaigns, but only one of these elicited a significant number of such responses. After asking doctors whether they believe "the mass education programs on such conditions as heart disease, cancer, and tuberculosis have served any constructive purpose" (to which 98% answered "Yes"), interviewers next asked, "Do you believe these programs have done any harm?" The majority of doctors (56%) answered, "No, no harm at all," but 44% answered "Yes," and almost all of these referred in one way or another to the arousal of fear.

Even though some 40% of the doctors declared that mass education programs do result in an increase, at least among certain segments of the population, in the prevalence of phobic concern with illness, only a very small number imply that the doctor-patient relationship is adversely affected by this increasing hypochondriasis. In fact, only slightly more than 2% indicated that the increase in fear has such boomerang effects as avoidance or distrust of physicians.

Moreover, when doctors were asked, "Are there any activities these (volunteer health) agencies carry out which you think ought to be curtailed or changed?" fewer than one doctor in 10 (only 7%) suggested less emphasis on fear of the disease in their information programs and fund-raising appeals. Actually, three-quarters of the doctors could not name any activity they would like changed or curtailed. In contrast, almost half of them had suggestions for expanding the activities of the voluntary agencies, and 17% suggested more public education.

Analysis of responses to these questions in terms of the doctor's age and the size of the community in which he practiced usually reveals only small differences. In general, the younger doctors and the big-city doctors were somewhat more approving of the cancer program, but, even among the older group and the small-town and rural group, the critics were generally a small minority. Thus, 81% of the doctors under 40 years of age endorsed the idea of semiannual pelvic examinations for all women over 35, but 67% of the doctors 40 or more years of age likewise expressed their approval.

Conclusions

There is, therefore, only a very small percentage of doctors who feel the American Cancer Society and similar agencies have done much harm and little good. There are some others who disapprove of particular aspects of the agencies' work. But most doctors are not at all reluctant to credit these agencies for the improved understanding and better health practices they have observed on the part of the public. Indeed, substantial numbers of doctors would urge the agencies to intensify their education programs and to expand their support of detection clinics and diagnostic services, as well as their support of medical research. It seems clear that the great majority of practicing physicians in the United States regard the major voluntary health agencies as useful allies in the continuing fight against ignorance and disease.

---

1. Anderson, O. W., with Feldman, J. J.: Family Medical Costs and Voluntary Health Insurance, New York, McGraw-Hill Book Company, Inc., to be published.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Pulmonary Stenosis and Ventricular Septal Defect with Arteriovenous Shunts: A Clinical and Hemodynamic Study of Eleven Patients. J. A. Callahan, R. O. Brandenburg and H. J. C. Swan. Circulation **12:**994-1004 (Dec.) 1955 [New York].

Patients who have pulmonary stenosis and ventricular septal defect usually have a right-to-left intracardiac shunt. This paper presents hemodynamic and clinical data on 11 patients who have pulmonary stenosis, ventricular septal defect, and left-to-right shunts. Four of these patients also have defects in the atrial septum, and three have demonstrable bidirectional shunts. The clinical diagnosis depends primarily on the diagnostician's being aware of the possible existence of a left-to-right intracardiac shunt with increased pulmonary blood flow in the presence of signs of pulmonary stenosis. All except one of the first seven patients had a harsh systolic murmur and thrill in the pulmonary area. The pulmonary arterial shadow was increased in all except one of these patients. Other physical signs, the pulmonary vascular markings, and the electrocardiograms were more varied. The technique of selection injections of T-1824, used in conjunction with measurements of blood oxygen saturation in the chambers of the heart and great vessels by cuvette oximeter, was of great value in the definition of the level, direction, and magnitude of intracardiac shunts. The decision about the form of treatment to be used in patients such as these should be based largely on hemodynamic considerations.

Is Insulin Deficiency the Same as Diabetes Mellitus? F. Gerritzen. Nederl. tijdschr. geneesk. **99:**3674-3680 (Dec. 3) 1955 (In Dutch) [Haarlem, Netherlands].

The late complications of diabetes such as cataract, retinopathy, arteriosclerosis, Kimmelstiel-Wilson syndrome (intercapillary glomerulosclerosis), and neuropathy are the chief problems for diabetic patients. Investigations into the underlying causes of insulin deficiency have suggested that complications may arise in three different ways: 1. An unknown factor may be responsible for insulin deficiency, which in its turn causes late complications. 2. The dominating influence of insulin antagonists (hypophysis, adrenals, or thyroid) may cause both the insulin deficiency as well as the complications. 3. The insulin deficiency as well as the complications may be due to the same unknown cause. Neither experimental studies nor clinical observations have clarified these problems, and the question remains whether diabetes mellitus and insulin deficiency are the same thing. It is possible that insulin deficiency is only one part of the clinical picture of diabetes mellitus. The author feels that, until it has been proved that diabetes, including its complications, can be produced in animals, it would be more correct to speak of "experimental insulin deficiency" rather than of "experimental diabetes." The author suggests that if obesity can be proved to be a factor in a relative insulin deficiency, it would be advisable first to relieve the excessive load on the pancreas by weight reduction and to give insulin as a secondary measure. If, on the other hand, excessive hypophysial, adrenal, or thyroid activities are causal factors in the insulin deficiency, efforts might be made to counteract this insulin antagonism. In this connection the author recalls that it has been proved experimentally that insulin deficiency can be improved by hypophysectomy (Houssay's phenomenon), adrenalectomy, and thyroidectomy. Any method designed to inhibit the functions of these endocrine organs (hypophysis, adrenal, or thyroid) might eventually prove helpful in the prevention of the complications of diabetes.

Cardiovascular Collapse in Acute Poliomyelitis. J. A. Hildes, A. Schaberg and A. J. W. Alcock. Circulation **12:**986-993 (Dec.) 1955 [New York].

During 1952 and 1953 a total of 1,359 patients were admitted to the acute poliomyelitis wards of the Winnipeg Municipal Hospitals. Of these, 523 had bulbar involvement and there were 82 deaths in the whole series. The immediate cause of death in 22 cases was cardiovascular collapse. These 22 cases and 6 others who survived after cardiovascular collapse in acute poliomyelitis are reviewed. Clinically, the syndrome came on acutely within one or two days after the onset of bulbar paralysis. It was characterized by apprehension, hyperthermia, and a fast, regular pulse and was sometimes preceded by a short period of hypertension. It then progressed to a state of shock with cold, sweating, and cyanosed extremities. Pulmonary edema was a common terminal feature. At autopsy, there was involvement of the medulla in all cases and pulmonary edema in all but one case. Interstitial myocarditis was found in 75% of the cases. Treatment with Noradrenaline appeared to be of benefit in some cases, but this was usually transient. Four of the six surviving cases had a mild form of the syndrome. It is suggested that the mechanism causing the syndrome is a combination of vasoconstriction resulting from a medullary lesion and a viral myocarditis. This leads to acute heart failure and pulmonary edema.

Etiology of Cancer of Esophagus. J. Mosbech and A. Videbaek. Nord. med. **55:**1845-1848 (Dec. 15) 1955 (In Danish) [Stockholm, Sweden].

The material studied comprises 101 cases of cancer of the esophagus, mostly histologically verified, in 83 men and 18 women. The average age at the onset was 67.9 for the men, 71.6 for the women. In fully half the cases the cancer was located in the middle of the esophagus, in about one-third it was in the lower part, and in about 10%, in the upper part. The marked preponderance of men is compatible with the assumption of exogenic origin and suggests that men are particularly susceptible to the cancerogenic action. The number of old patients suggests that the cancer-accelerating factor has a long latent period or is present for a long time before the carcinoma develops. Cancer of the esophagus is attributed essentially to exogenic factors. Excessive drinking was important etiologically: 65% of the men were alcoholics and 21% were exposed occupationally to alcohol. There was no correlation between syphilis and cancer of the esophagus. Hereditary factors seemed to be of no etiological significance.

Acquired Haemolytic Anaemia: Clinical and Serological Observations of Two Cases. W. Weiner, J. P. Whitehead and W. J. Walkden. Brit. M. J. **1:**73-77 (Jan. 14) 1956 [London, England].

Two cases of acquired hemolytic anemia are described in a 47-year-old man and a 50-year-old woman. The two patients presented different clinical and hematoserologic pictures. In the man, chest x-ray examination revealed patchy infiltration in the left upper lobe of the lung, suggestive of pneumonia or tuberculosis. Slight improvement in the appearance of the lung in the roentgenogram resulted from combined treatment with streptomycin and aminosalicylic acid (PAS), but there was growing clinical evidence of periodic exacerbations of the patient's

---

The place of publication of the periodicals appears in brackets preceding each abstract.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by individuals in continental United States or Canada who subscribe to its scientific periodicals. Requests for periodicals should be addressed "Library, American Medical Association." Periodical files cover 1947 to date only, and no photoduplication services are available. No charge is made to members, but the fee for others is 15 cents in stamps for each item. Only three periodicals may be borrowed at one time, and they must not be kept longer than five days. Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

illness with loss of appetite, vomiting, and increased jaundice. An active hemolytic process was revealed by the examination of the patient's blood, which showed 10 gm. hemoglobin per 100 cc. (68%) and 10% reticulocytes. The patient's reaction to the direct Coombs' test was strongly positive, and the serum bilirubin determination was 4.1 mg. per 100 cc. The urine contained an excess of urobilinogen. Treatment with cortisone was started with 300 mg. daily, and the dose was gradually reduced to 150 and 100 mg. daily while the patient improved steadily. On repeated examination, his hemoglobin level was 12.7 gm. per 100 cc. (85%) and the reticulocytes were 3.6%. The daily dose of cortisone was gradually reduced to 37.5 mg., which seemed to be sufficient to maintain the patient's hematological values. In the woman, x-ray examination of the chest did not reveal any abnormality. She was moderately jaundiced and had widespread ecchymoses and purpura. Examination of the blood revealed that the hemoglobin level was 3.55 gm. per 100 cc. (24%), and there were 26% lymphocytes, 1% monocytes, 3% late normoblasts, and 50% reticulocytes. There were less than 1,500 blood platelets per cubic millimeter. This patient thus showed the not unusual association of acquired hemolytic anemia with thrombocytopenic purpura. As the anemia endangered the patient's life, an emergency transfusion of 1,140 cc. of group A rhesus-positive blood was given, but it produced only very temporary improvement. Cortisone therapy was started with 300 mg. of the drug given daily, with resulting rapid improvement. After two months of treatment with cortisone the patient was discharged on a maintenance dose of 25 mg. of cortisone daily. After an infection of the upper respiratory tract, she had a further hemolytic crisis requiring readmission, to hospital, but she again responded satisfactorily to cortisone therapy and was discharged on 75 mg. of cortisone daily. Another cold was followed by another severe hemolytic crisis, but an increase of the cortisone dosage produced a clinical remission and the patient remained well on therapy with 62.5 mg. daily. Serologic studies were carried out in both patients. Because of the established connection between acquired hemolytic anemia and virus pneumonia, the serum of the man was investigated for the presence of antiviral antibodies, and, though nothing significant was found, it is tempting to think that a virus may have played some part in the causation of his disease. An anti-E antibody was present in the serums and eluates of both patients, whereas an anti-c antibody could be recovered from the eluate only of the woman. It would appear to be imperative to use not only the serum but also the eluate for cross matches in selecting blood, if transfusion treatment is decided on in patients with acquired hemolytic anemia. Although dramatic transfusion reactions do not occur frequently in patients with acquired hemolytic anemia even if the eluate and/or the serum contains the homologous antibody against the antigen introduced by the transfusion, there is no doubt that the blood the patient is given is very rapidly destroyed and no benefit results, as happened in the woman patient. Cortisone therapy in both patients was effective in controlling the hemolysis, and both patients achieved a good remission.

SURGERY

Surgical Treatment of Achalasia of the Esophagus. R. H. Sweet. New England J. Med. **254:**87-95 (Jan. 19) 1956 [Boston].

Forty-eight patients between the ages of 2 and 74 years with achalasia of the esophagus were operated on in the course of 10 years. There were 29 females and 19 males. Primary resection was performed on the first six patients because of a coexisting gastric ulcer, and in six others a secondary resection was performed because of the failure of a previous surgical procedure. Experience with these 12 patients suggested the existence of two distinct types of achalasia of the esophagus: the type in which there is a thin atrophic muscle layer at the lower end of the esophagus, which should be treated by an esophageal esophagoplasty with a longitudinal incision and circumferential closure; and the type in which the distal segment of the esophagus is characterized by hypertrophy of the circular muscle fibers, which should be treated by an esophagomyotomy (modified Heller operation). An esophagoplasty was performed in 26 patients and an esophagomyotomy in 10. There were two postoperative deaths among the 26 patients subjected to esophagoplasty; one of these deaths resulted from a transfusion of mismatched blood, and the other resulted from uncontrollable hemorrhage into the gastrointestinal tract caused by diffuse severe gastritis and esophagitis in a 74-year-old man who was in poor condition because of inanition. None of the 10 patients treated by esophagomyotomy died after operation. Of the 46 patients who survived the various operations, 2 died of unrelated causes long after the operation performed for relief of achalasia. A follow-up of 34 patients was carried out for three or more years after the operation. It was based on the patient's own estimate and the findings on x-ray examination and esophagoscopy by two examiners. This study revealed excellent results, with 90 to 100% improvement in 19 patients; good results with improvement estimated to be 80 to 90% of normal in 9 patients who were essentially well, holding responsible jobs and suffering only minor or occasional inconveniences; fair results with improvement about 70 to 80% of normal in 4 patients; and poor results with less than 70% improvement in the remaining 4 patients, 2 of whom bled so extensively from gastritis that a resection had to be performed and 2 of whom had stenosis at the site of an esophagoplasty that required bougienage for relief. The results of esophagomyotomy were entirely satisfactory. The four patients in whom results were poor had been treated by esophagoplasty. In 3 others so treated there were only fair results, but in 13 of the 20 followed there were excellent or good results. The failure to realize the importance of restoring normal relations of the gastric cardia and the diaphragm at the esophageal hiatus in some of the earlier cases accounted for some of the disappointing results in this group. Good to excellent results were obtained in the group subjected to resection, with no poor results and only one fair result. Delayed emptying of the stomach caused by altered motility and spasm of the antrum and pylorus, which may be an accompaniment of the disease or which may develop after certain operations (notably resection involving interruption of both vagus nerves), must be treated by pyloroplasty to avoid the untoward or actually hazardous effects of delayed gastric emptying. At least 80% of patients operated on for achalasia of the esophagus should have good to excellent results.

Total Adrenalectomy and Oophorectomy for Carcinoma of the Breast. K. Cuningham. M. J. Australia **2:**1021-1024 (Dec. 17) 1955 [Sydney, Australia].

The author performed total adrenalectomy and oophorectomy in 30 women with metastatic breast cancer within the last two years. If the nutritional status of the patient is poor or if she is vomiting, admission to the hospital for one or two weeks is desirable. A vitamin-rich diet combined with cortisone therapy will improve the patient's general condition. Otherwise, admission to the hospital 48 hours prior to operation is sufficient. The author has learned that bilateral adrenalectomy in one stage is a dangerous procedure. No patient should be subjected to this risk unless she has refused to accept the operation in two stages. The first stage consists of bilateral oophorectomy and usually left adrenalectomy. Seven to 14 days later the other adrenal is removed. Full cortisone therapy is given in the 24 hours preceding each operation. As the adrenal vein is about to be ligated, the anesthetist gives 50 mg. of cortisone. If the blood pressure falls and remains below 110 mm. Hg systolic and 75 mm. diastolic, Methedrine or extra cortisone is given. With the two-stage procedure, convalescence is uneventful. Replacement is maintained by the administration of 37.5 to 50 mg. of cortisone given daily by mouth. In the author's experience, 90% of patients experience subjective improvement, as demonstrated by improved nutrition, more cheerful mental outlook, and ability to care for their own needs and those of their family; this is maintained until within a few days or weeks of death. Death does not occur by a slow process of attrition and cachexia, but is usually sudden and caused by acute irreversible adrenal failure, when replacement therapy with cortisone loses its effect. There is a 50% chance of objective reduction in established metastases. In the author's opinion, it is the treatment of choice in premenopausal women with metastatic breast cancer.

Management of Patients with Portal Hypertension Undergoing Venous-Shunt Surgery. W. C. Ebeling, J. P. Bunker, D. S. Ellis and others. New England J. Med. **254:**141-148 (Jan. 26) 1956 [Boston].

A study of the operative and immediate postoperative response of patients with portal hypertension and liver disease to venous-shunt surgery is presented (1) to provide prognostic criteria for the selection and management of this particular group of patients and (2) for the management of any patient with chronic liver disease undergoing major surgery. There were 129 patients, all but 6 of whom had bled massively from esophageal varices. Portal hypertension was caused by cirrhosis in 100 patients and by extrahepatic portal-bed block (Banti's syndrome) in 29. Preoperative studies included determination of bromsulphalein retention; serum albumin, bilirubin, and alkaline phosphatase concentration; cephalin-cholesterol flocculation, and one-stage prothrombin time. Preoperative preparation emphasized diet, rest, and, when indicated, whole blood transfusions and intravenous administration of human albumin. There were 83 splenorenal, 36 portacaval, and 6 "makeshift" shunts and 16 unsuccessful attempts to construct a shunt. Surgery was performed with the patient under ether, cyclopropane, or, more recently, hypotensive spinal anesthesia. Postoperative treatment included administration of oxygen by nasal catheter for 24 to 48 hours and the administration of adequate amounts of hypertonic dextrose solution intravenously, as well as support of fluids, electrolytes, and red blood cell volume. Serious operative or postoperative complications directly related to the liver occurred in 27, or 19%, of the operations. Liver failure developed in 22 patients, 8 of whom died. Five patients died during surgery of uncontrollable venous and capillary bleeding (all five in the first five years of the study—1945-1949—before the use of fresh blood became routine during shunt surgery). All but two of these complications were in patients with cirrhosis. The correlation of laboratory and physical findings with clinical results provided additional prognostic criteria. Preoperative bromsulphalein retention of 10% or less gave a virtual (98%) guarantee of freedom from postoperative liver complications. Conversely, a low preoperative serum albumin level (below 3.0 gm. per 100 ml.) was associated with a prohibitively high (66%) rate of hepatic complications. Preoperative disturbances in other liver-function tests were of less specific prognostic value. The choice of operation was important in determining the outcome. Postoperative liver failure in cirrhosis occurred twice as often after a portacaval as after a splenorenal anastomosis. The choice of anesthetic agent had surprisingly little effect on the outcome. Liver failure followed cyclopropane anesthesia as often as it did the use of ether. The experience with hypotensive spinal anesthesia, used in most of the recent cases, has been as good as that with ether or cyclopropane, and, in view of the extraordinary technical difficulties of shunt surgery, induced hypotension is probably justified in cases in which there are no obvious contraindications.

Follow-Up Studies of Iliofemoral Arterial Reconstruction in Arteriosclerosis Obliterans. S. J. Hoye and R. Warren. New England J. Med. **254:**102-106 (Jan. 19) 1956 [Boston].

Thirty-one operations for primary arterial reconstruction in the iliofemoral arterial trunk were performed on the extremities of 29 men between the ages of 32 and 73 years, 2 of whom underwent operations on both extremities. Intermittent claudication was the major presenting symptom in 22 extremities; there was objective evidence of tissue breakdown in 6 extremities, and rest pain in 3 extremities. The types of reconstruction were 16 arterial homografts, 12 saphenous vein autografts, 1 superficial femoral vein autograft, and 2 thromboendarterectomies. The two thromboendarterectomies were performed early, and both reoccluded within the period of hospitalization. There were no operative or hospital deaths. Six patients were reoperated on within 24 hours after the first intervention. These reoperations were performed for thromboses and hemorrhages, occurring in two patients each, and because of doubtful arterial inflow immediately after operation in the remaining two patients. All but 3 of the 29 patients who had grafts inserted left the hospital with a patent graft. Of the 16 arterial grafts, 9 closed within seven months. Of the 13 autogenous vein grafts, 8 reoccluded, 6 within six months and the other 2 at eight and nine months. Of the 29 grafts, 7 were performed within the six months immediately before the termination of the authors' study; at present there are five patent grafts in this group. Twenty-two patients with grafts were followed for six months or more, with 2 of 9 arterial grafts and 5 of 13 venous grafts maintaining patency, giving a rate of 32% for patency in those followed over six months. The various factors that may contribute to late closure offer no substantial clue to the cause. The finding of disseminated, partially occluding organized thrombi in the occluded grafts was striking. Despite the high incidence of later failure of these reconstructions, the authors still advise the procedure for any person who is prevented by ischemic symptoms from participating in the normal activities of his age group. The use of lumbar sympathectomy as a preliminary measure is wise as a protection against later graft closure.

Use of Grafts in Treatment of Atherosclerosis of Lower Limbs. R. E. Horton. Brit. M. J. **1:**81-82 (Jan. 14) 1956 [London, England].

Twenty-nine patients with segmental obstruction of the arteries to the lower extremities caused by atheroma were treated by grafting and followed for periods up to three years. Twenty-five grafts consisted of homologous adult arteries, two were of homologous fetal aorta, and two were of autogenous saphenous veins. The operations were performed for intermittent claudication severe enough to keep the patient from his work and for rest pain associated with minor degrees of necrosis. The end-to-end technique was used in all cases. There were three deaths: two patients with generalized disease and advanced gangrene died of coronary thrombosis, and one patient died of hemorrhage caused by a leak from the suture line of an iliac graft while being treated with heparin. This gives a mortality rate of 10%, but with proper selection of patients, excluding those with generalized disease and gangrene, the mortality should be negligible. Of the 26 patients who survived the operation, 7 had iliac and proximal femoral artery grafts; early thrombosis did not occur in any of these patients, and late thrombosis occurred in only one. Nineteen patients had distal femoral and popliteal artery grafts; early thrombosis occurred in 10 and late thrombosis in 6. The high failure rate in the second group of patients leads to the conclusion that grafting of the distal femoral and popliteal arteries by the technique employed is not worth while, though it is possible that the end-to-side operation may give better early results. The results of grafting the proximal femoral and iliac arteries were much more satisfactory.

Fatal Enterocolitis Due to Antibiotics: A Report of Three Cases. J. A. K. Cuningham and D. W. Beaven. New Zealand M. J. **54:**644-647 (Dec.) 1955 [Wellington, New Zealand].

The authors present the histories of and postmortem studies on three patients in whom fatal enterocolitis developed after treatment with antibiotics. In the first, fatal enterocolitis developed after treatment with Aureomycin, in the second after the use of a combination of penicillin and streptomycin followed by Terramycin, and in the third after the use of erythromycin. The use of penicillin and streptomycin in combination or one of the broad-spectrum antibiotics alone results in a profound disturbance of the intestinal flora with a marked decrease in the bacterial population. If the patient harbors a resistant Micrococcus (Staphylococcus) in the nasopharynx, this organism may multiply and fill the "bacteriological vacuum" in the bowel. Micrococcic enterotoxin is produced and gives rise to vomiting, diarrhea, and collapse. In micrococcic food poisoning, preformed enterotoxin is ingested, but the symptoms are self-limiting, as no further toxin is produced in vivo. However, in micrococcic enterocolitis after antibiotic therapy, organisms continue to multiply and produce toxin. Patients whose intestinal tracts have been well sterilized prior to intestinal surgery appear to be particularly liable to this complication in the postoperative period. The development of diarrhea in a patient under treatment with a broad-spectrum antibiotic should lead one to suspect the condition. In the majority of cases the diarrhea decreases when the antibiotic is discontinued. If a fecal smear reveals gram-positive cocci and there is deterioration in the patient's condition, erythromycin should be promptly administered.

Unfortunately, micrococci all too readily develop resistance to erythromycin. For this reason it should not be used as a primary treatment but might well be reserved for cases of micrococcic enterocolitis or other micrococcic infections due to resistant strains. If it is employed indiscriminately, we may lose one of our most effective weapons in the treatment of resistant micrococcic infections.

Acute Enterocolitis as Postoperative Syndrome. O. Scholz. Beitr. klin. Chir. **191:**418-426 (No. 4) 1955 (In German) [Munich, Germany].

Six cases of postoperative acute enterocolitis were observed in the course of the last three years at the surgical clinic of the University of Leipzig. Five of the patients had undergone resection of the stomach and the sixth cholecystectomy and choledochotomy. The six patients died, and the autopsy findings are enumerated. Microscopic studies on the intestine revealed superficial necroses of the mucosa. Other specimens revealed that the mucosa in some areas was covered by a pseudomembrane consisting of fibrin, cellular detritus, and sheets of bacterial colonies. A survey of case histories and autopsy records failed to reveal this serious postoperative complication as a cause of death during the years from 1946 to 1951. The author agrees with other investigators that acute postoperative enterocolitis has become more frequent. It does not respond to treatment and is usually fatal in from two to four days. Allergic factors might be involved in the etiology, and antihistaminics might prove of value in the therapy. It is also suggested that the broad-spectrum antibiotics could play a part in acute postoperative enterocolitis (1) by their secondary antigenic actions; (2) by producing therapy-resistant bacterial strains; and (3) by destroying the natural bacteriological intestinal flora and thus promoting superinfection.

NEUROLOGY & PSYCHIATRY

Treatment of Senile Agitation with Chlorpromazine. L. A. Terman. Geriatrics **10:**520-522 (Nov.) 1955 [Minneapolis].

Therapy with chlorpromazine was tried in 22 persons who were considered to be among the more intractable in a group of agitated senile patients. Their ages ranged from 72 to 93 years. All had exhibited symptoms of agitation for six months or more and some for as long as 10 years. Treatment was started with a low dosage of 10 mg. of chlorpromazine given orally three times a day. If the patient did not show improvement on this dosage, it was increased to 25 mg. orally or intramuscularly three times daily. The larger dosage usually induced drowsiness and lethargy, so that, when the desired results were obtained, it was decreased to 10 mg. Since hypotensive responses are more likely to occur when chlorpromazine is administered intramuscularly, this form of dosage was used only when patients refused to take the drug by mouth. After only one week of therapy, 21 of the 22 patients became manageable, ate and slept better, and responded well to the institutional routine. It is a wise precaution to keep patients in a prone position and check blood pressure frequently for one hour after each of the first few doses of the drug. Results obtained in this group would indicate that chlorpromazine is a relatively safe and useful drug for improving manageability of the agitated senile patient.

Use and Abuse of Hypnotics. M. H. Wulff. Ugeskr. læger **117:** 1639-1647 (Dec. 15) 1955 (In Danish) [Copenhagen, Denmark].

The abuse of hypnotics must be viewed in connection with the whole problem of narcomania. The causes of the frequent use and abuse of hypnotics are manifold. Constitutional factors and social relations and habits are involved. An increase in the number of patients in Denmark hospitalized because of drug addiction is largely due to abuse of hypnotics, particularly amobarbital (Pentymal). General use of Pentymal in Denmark began in 1951. It is rapidly eliminated and is employed primarily as a sedative. Whether Pentymal is more likely to result in psychic and physical dependence than other barbiturate substances is not known. Abstinence symptoms occur more quickly after Pentymal than after Phenemal, and there can hardly be any doubt that the patient is more likely to continue its use and eventually increase the dose. It has been used more and more for euphorizing purposes. Eighty-five patients addicted to hypnotics were closely examined with regard to abstinence symptoms, and 22 had convulsions. Twelve of these were also temporarily psychotic, and psychotic reactions developed in four additional patients. A definite tendency to abstinence symptoms is seen after abuse of a substance with rapid elimination. It must as a rule be considered dangerous to administer hypnotics as sedatives during the day time. The indications are that both psychic and physical habituation occurs more easily when the sedative is given during the day. Sedatives should not be prescribed for day time to constitutionally asthenic and labile persons, patients with chronic neuroses, or alcoholics.

Chronic Barbituric Acid Abuse: A Euphomania Problem. A. Myschetzky. Ugeskr. læger **117:**1647-1649 (Dec. 15) 1955 (In Danish) [Copenhagen, Denmark].

From 1949 to 1954, inclusive, 269 patients (100 men, 169 women) were admitted to the psychiatric department of Bispebjerg Hospital because of chronic barbituric acid abuse. There were nine times as many admissions in the last year as in the first year. Abstinence symptoms occurred in 10% of the patients, and about 7% had abstinence psychoses. While Allypropymal was the hypnotic most often abused, there was a marked increase in the use of Pentymal. This substance seems most often to lead to euphoria. The danger of habituation and craving is considerable with all barbituric acid preparations.

PEDIATRICS

Coarctation of the Aorta with Congestive Heart Failure in Infancy—Medical Treatment. H. T. Lang and A. S. Nadas. Pediatrics **17:**45-57 (Jan.) 1956 [Springfield, Ill.].

Five girls and four boys between the ages of 12 days and 13 months with coarctation of the aorta and congestive heart failure were studied. The infants had feeding problems consisting of anorexia, vomiting, and fatigue during feeding. They failed to thrive. Dyspnea and cyanosis were observed. In addition to the finding of a blood pressure in the upper extremities at least 20 mm. Hg higher than that in the lower extremities, which was related to the coarctation itself, signs of both left-sided and right-sided congestive heart failure were noted. The latter consisted of pulse rates greater than 150 beats per minute, sinus tachycardia, and increased respiratory rate. Roentgenograms of the chest revealed generalized cardiac enlargement and passive congestion of the lungs. Electrocardiograms obtained from infants less than 6 months of age showed left, right, or combined ventricular hypertrophy, whereas those obtained from children over 6 months of age all showed left ventricular hypertrophy. Since there is little assurance that after early surgical intervention on the narrowed or constricted aorta the growth of the anastomotic site will keep pace with that of the infant, and because of the high operative mortality, the infants reported on were treated medically. Digitoxin in doses of 0.033 to 0.066 mg. per kilogram of body weight was given within a 24-to-36-hour period in divided doses. One-tenth of the digitalizing dose was given every day for maintenance. Meralluride (Mercuhydrin) sodium intramuscularly in doses of 0.25 cc. and a sodium-free formula, Lonolac, were given to two infants who appeared edematous. Oxygen and broad-spectrum antibiotics were administered to every infant. The immediate results of this treatment were gratifying. All infants survived. The irritability and evidence of congestive failure subsided. The patients were discharged within two to three weeks after admission, and digitalization was maintained throughout infancy. The patients were followed up for periods varying from three months to five years. These children were doing well and were free of symptoms. Although they tended to be somewhat short in stature, their nutritional state was satisfactory. These results suggest that congestive failure in infants with uncomplicated coarctation of the aorta can be treated satisfactorily by medical means until the patients reach late childhood or early adolescence, at which time complete and probably permanent surgical relief of the aortic coarctation can be performed with an operative mortality of less

than 5%. Surgical treatment, however, should be practiced early if medical management fails or if signs of hypertensive encephalopathy develop.

Rheumatic Disease in Infancy: Clinical and Statistical Findings in 112 Cases. E. Segagni. Minerva pediat. **7**:1309-1318 (Oct. 27) 1955 (In Italian) [Turin, Italy].

A review of the 112 cases of rheumatic disease seen at the Pediatric Clinic of the University of Turin from 1946 to 1954 revealed that most cases occurred toward the end of winter and the beginning of spring and that the disease affected mostly children of the school age group (average age, 7.98 years). There were 53 boys in this series. A familial history of rheumatic disease could be found in 51 instances. The first phase of the disease was characterized by a streptococcic infection in 43.72% of the cases. The so-called latent period, i. e., the time elapsed from the occurrence of the infection to the onset of the first symptoms, ranged from one week to about three months. Polyarthritis was present in 86.61%, and the joint most frequently involved was the knee joint. Concurrent myalgia was present in 1.8% and neuritis in 2.68% of the patients. Carditis was found in 44.15% of the patients at the time of the first attack, and in 69.69% during the subsequent attacks. If the patients with a slight heart impairment are added, it was present in 90.26%. As a rule, the electrocardiographic findings were altered. Roentgenograms showed enlargement of the heart only in the patients with acute carditis. Cardiac decompensation was observed in 8.92%. Chorea minor was present in 17 patients, most of them girls. Erythema nodosum was seen in 4.46% and nosebleed in 18.9%. Fever was present in all the patients, was more or less elevated, and disappeared by lysis. The erythrocyte sedimentation rate was always increased, the hemoglobin level was decreased in 88%, and the red blood cell count was less than 3,500,000 per cubic millimeter in 51.3%. Leukocytosis with neutrophilic polynucleosis was present in 69%, leukocytosis with mononucleosis in 23.5%, leukopenia in 67%, and eosinophilia in 50%. At the author's clinic treatment consisted mainly in the administration of antibiotics and sulfonamides. Salicylates were also given concurrently by the oral, rectal, or transpulmonary route. In the severest cases corticotropin was also administered. A complete recovery was obtained in 31.47%; residual heart impairment was observed in 40.67%; in 20.3% the disease had a stormy course, recurred, and caused heart decompensation; and 7.4% died from cardiac decompensation. The average hospital stay was 49.26 days.

The Nature of the Hyaline Membrane in Asphyxia of the Newborn. D. Gitlin and J. M. Craig. Pediatrics **17**:64-71 (Jan.) 1956 [Springfield, Ill.].

The lungs of five newborn infants of 27 to 40 weeks' gestation who died because of respiratory difficulty associated with the formation of pulmonary hyaline membranes were studied by fluorescent antibody and dye-staining procedures. Five different samples of human amniotic fluid obtained by aspiration at the time of elective cesarean section and through the vagina in two cases of artificial rupture of the membranes were studied by the same methods. The hyaline membranes in these infants were composed largely of fibrin. Although small amounts of fibrin were found in some of the amniotic fluids studied, the quantities were small relative to those found in the membranes. Since insoluble fibrin cannot be transferred across capillary or cellular membranes as such, the fibrin must have formed in the alveoli or alveolar ducts. The transcapillary migration of fibrinogen, even with normal capillary permeabilities, has been described by other workers. The presence of the fibrin membrane in the alveoli indicates effusion from the pulmonary circulation as the first step in the development of pulmonary hyaline membranes in the human infant. The conversion of fibrinogen in the effusion to fibrin is the second step, and it is a process that would be enhanced by, but would not necessarily depend on, the presence of thromboplastic material in aspirated amniotic fluid. The third step may be syneresis of the fibrin network to form a membrane. This concept does not imply that the entire membrane as seen in the five infants reported on was composed only of fibrin; fat and squamous cells were also present in significant amounts originating from vernix caseosa in the amniotic fluid.

Artificial Hibernation in Pediatrics: Its Application in Toxic Infections of Nurslings. M. Crisalli, S. Scarabicchi and A. Terragna. Minerva pediat. **7**:1318-1333 (Oct. 27) 1955 (In Italian) [Turin, Italy].

The authors report good results in seven of nine nurslings with grave toxic infections in whom, other therapies having failed, artificial hibernation was induced according to Laborit's method. The infants' ages ranged from 48 days to 11 months. Three of them had toxic gastroenteritis without marked parenteral morbid processes; three, toxicosis with bilateral antritis; two suppurative otitis, one of them with convulsions and dermatitis of the Kaposi type; and one, hyperthermia in the course of myocarditis and suppurative otitis. The hibernation was prolonged for from a minimum of 20 hours to a maximum of eight days, the latter in two patients with bilateral antritis and severe dystrophy with marked toxemia. Undesired effects observed during the treatment were slight tremor of the hands and onset of tympanites in two infants; marked bronchial secretion, which continued for a few days after the treatment in one case; slight melena in one; and generalized edema, which disappeared as soon as the introduction of fluids was suspended, in one case. The internal temperature reached was never low; as a rule, a temperature of 34 C (93.2 F) was sufficient to produce attenuation of the toxic state. In only one instance was a temperature of 31 C (87.8 F) reached. In the seven patients who were greatly benefited by the treatment, vomiting, diarrhea, and convulsions disappeared; they were put back on their usual feedings, and thus they recovered quickly. Two infants died; in one of them, who had latent bilateral antritis, the infection reappeared after the treatment was suspended, and the other died during the induction of artificial hibernation, probably because of a myocarditis. The authors conclude that artificial hibernation seems to be the treatment of choice for toxic infection of infants, provided continuous medical surveillance is available. The treatment should be individualized.

Edema of Newborn Infants: Case of Sclerema Neonatorum Successfully Treated with Corticotropin. P. V. Nuñez. Arch. méd. paname. **4**:157-160 (July-Aug.-Sept.) 1955 (In Spanish) [Panama, R. de P.].

Sclerema neonatorum is a rare disease. It was considered rapidly fatal until the discovery of corticotropin and cortisone. Patients successfully treated with either of these hormones have been reported in the literature. The disease occurs only in premature infants and in those with congenital debility. The symptoms are diffuse hardening and tightness of the skin and severe depression of respiration. The subject of this report weighed 6 lb. at birth. The mother had edema in pregnancy; she died two hours after parturition, with convulsions. When the infant was 15 days old he had diarrhea and dehydration. He lost 2 lb., constantly moaned, and became very ill, with dyspnea. He was put in an oxygen tent and was fed by gavage with skimmed milk and kept warm with warm bags. For the first two days the treatment consisted of oral administration of streptomycin in doses of 200 mg. every six hours, a subcutaneous injection of 150 cc. of a solution containing sodium chloride, sodium lactate, and phosphates of calcium and potassium (Hartmann's solution), and, on the second day, an enema of Ringer's lactate and subcutaneous administration of a 5% dextrose solution. The rectal temperature fell suddenly to 36 C (96.8 F), the patient became cyanotic, and his body became cold and rigid. The treatment consisted of ACTH by parenteral route in doses of 5 mg. every six hours, Terramycin in doses of 50 mg. every six hours, and nikethamide. Feeding with skimmed milk was continued by gavage. Improvement progressed slowly for two days and rapidly for the following week until there was complete disappearance of cyanosis and dyspnea, restoration of skin and subcutaneous tissues to normal texture, and restoration of the ability of the patient to suck. The total dose of ACTH was 40 mg. There were no complications during convalescence. The patient was discharged one month later as normal, weighing 6.5 lb. The author concludes that edema of newborn infants frequently is the result of the parenteral administration of sodium chloride solution given in the treatment for dehydration. Treatment should be given by mouth. When the parenteral route is resorted to, weak electrolyte solutions should be used and given at certain

intervals. Either ACTH or cortisone is of value in the treatment of sclerema neonatorum, as observed in the case reported by the author.

THERAPEUTICS

Biliary Stasis Produced by Chlorpromazine: An Experimental Study. R. B. Menguy, J. L. Bollman, J. H. Grindlay and J. B. Cain. Proc. Staff Meet. Mayo Clin. **30**:601-606 (Dec. 14) 1955 [Rochester, Minn.].

The administration of chlorpromazine (Thorazine) is complicated in some patients by the onset of jaundice that seems to be of the obstructive type. Since this implies stasis in the biliary tree, the authors investigated the effects of chlorpromazine on the resistance of the choledochoduodenal sphincter as well as on the biliary intraductal pressure in mongrel dogs. They found that chlorpromazine administered to dogs in doses of 10 mg. per kilogram of body weight produces stasis in the biliary tree due to an increase in the resistance of the choledochoduodenal sphincter. These changes appear to be related to the depressing effects of chlorpromazine on duodenal motility.

Anaphylactic Penicillin Reactions: Three Nonfatal Cases of Reaction to Oral Penicillin with Positive Skin Tests and One Fatal Case Following Intramuscular Penicillin. G. A. Peters, L. L. Henderson and L. E. Prickman. Proc. Staff Meet. Mayo Clin. **30**:634-640 (Dec. 28) 1955 [Rochester, Minn.].

Oral administration of penicillin is not without hazards. The first patient reported on came to the Mayo Clinic because of two attacks of unconsciousness. She had frequently used penicillin troches or tablets for minor ailments. She had taken a 100,000-unit tablet of penicillin for a sore throat immediately prior to the first attack. She lost consciousness within 15 minutes. Oxygen was administered, and she roused in 45 minutes but appeared dazed for several hours. Two months later the patient took two tablets of penicillin with the same result. A patch test to penicillin caused no local reaction, but a scratch test, using a drop of solution containing 20,000 units of penicillin G per milliliter, produced a large erythematous area with whealing and pseudopod formation. During the next 20 minutes the patient experienced tingling in the tongue, palpitation, generalized flushing and weakness. She recalled that she had noticed similar symptoms shortly after the patch test had been applied. The second patient gave a history of two episodes in June and September, 1955, characterized by dryness of the mouth, choking sensation, tightness of the chest, nausea, vomiting, diarrhea, faintness, and unconsciousness. She had undergone thyroidectomy in May, 1955, after which she received a penicillin-streptomycin combination for 4 days. Two weeks postoperatively the first attack occurred. The patient improved as oxygen was given. The second attack occurred within two minutes after she had taken a buffered penicillin (250,000 units) tablet for a mild pharyngitis. Scratch tests were performed with penicillin G in dilutions of 5,000 and 20,000 units per milliliter, and each produced severe erythema and whealing. Serum was obtained for passive-transfer tests that also proved positive when challenged with varying quantities of penicillin G, ranging down as low as 1 unit. The third patient had not felt well since a severe penicillin reaction more than a year previously. Prior to that time she had taken oral troches and intramuscular injections of penicillin with impunity. Her first attack occurred within 15 minutes after she had received an intramuscular injection of penicillin for an upper respiratory infection. Widespread angioedema and urticaria developed so that she could hardly breathe, and facial edema was so severe that she could not see. About a year later, after a dental extraction, she was given some pink tablets. After arriving home she put a tablet in her mouth and in less than a minute experienced generalized tingling and burning, and her hands, feet, face, and tongue became swollen. She began to choke and felt herself losing consciousness. She regained consciousness after oxygen administration. She refused direct skin testing but permitted blood to be withdrawn for passive-transfer tests that proved positive with as little as 10 units of penicillin G. The fourth patient, in whom an intramuscular injection of 600,000 units of procaine penicillin was followed by death, had no history of ever having had penicillin, but she had been asthmatic for two years. Penicillin should be used with discrimination. It should not be used for uncomplicated colds, virus infections, or sore throats. If the patient has an allergy to penicillin, it is best to avoid the drug entirely.

PATHOLOGY

The Pathology of Severe Digestive Esophagitis. P. M. Peters. Thorax **10**:269-286 (Dec.) 1955 [London, England].

The author describes studies made on specimens derived from 20,000 autopsies. During the two years of the investigation (1950 and 1951) specimens of esophagitis were specially collected, the routine autopsy technique often being modified so that esophagus, stomach, and diaphragm were removed in one. The histological reports and the cause of death in all cases indexed as ulceration or inflammation of the esophagus were traced; cases of esophagitis not due to peptic digestion were then eliminated. Slides of the remainder were examined, fresh sections being cut if necessary, and all slight or doubtful lesions and some with complicating elements, e. g., deep thrush infection, were then excluded. After this double selection, 116 cases remained. The essential facts concerning each patient were then assembled from the clinical and pathological records. Peptic, reflux, or digestion esophagitis may be defined as inflammation of the esophagus due to digestion by gastric secretions. Reflux esophagitis and peptic esophagitis are the terms most in use today. The former is open to the criticism that it describes an indirect and not the direct cause and that it does not include the possibility of digestion by the secretions of proximal ectopic gastric mucosa; also, reflux suggests a passive state, not vomiting, a common predisposing condition. Digestion esophagitis, Quincke's original term, seems both accurate and convenient. Indirect causes are those that allow enough gastric juice to be present in the esophagus for digestion to occur. In this series they were arranged into extrinsic and intrinsic groups in relation to the cardial closure mechanisms. Extrinsic factors were persistent vomiting and nausea and increased intra-abdominal pressure. Intrinsic factors were acquired hiatal hernia, congenital enlargement of the hiatus and congenital shortness of the squamous esophagus, mechanical interference with the crural tunnel, and organic lesions, e. g., ulcer or carcinoma, of the gastric cardia or high on the lesser curve. Primary abnormalities of the hiatus of the diaphragm associated with hiatal hernia are congenital enlargement, atrophy (often senile), and toxic laxity; the last two are probably common causes of esophagitis, especially when influenced by posture (bending over or lying supine), but are difficult to assess in a pathological survey. The interrelationship of vomiting and reflux, esophageal shortening, esophagitis, and hiatal hernia is complex. It seems that persistent vomiting and reflux can cause hiatal hernia (by spasm shortening), and hiatal hernia due to primary abnormalities of the diaphragm can cause vomiting and reflux. Both these sequences are associated with digestion esophagitis. Gastric or duodenal ulcers were present in practically one-third of the series (29.2%). Most, if not all, such patients have hyperchlorhydria at some stage, and, as hyperacid juice digests living tissue much faster than normal juice, highly acid vomit or reflux is more likely to cause esophagitis. Multiple predisposing factors were common (42.5%). At any stage of the disease death may follow perforation into the mediastinum, pleura, pericardium, or, if the leak is below the hiatal elastic ligament, into the upper abdomen. There is general liability to aspiration bronchopneumonia. A patient may become grossly anemic from chronic or intermittent oozing from raw surfaces. Patients may have much pain and fear of eating or adopting certain postures. Some patients are labelled neurotic because their persistent complaint of indigestion is coupled with negative radiographs of stomach and duodenum. Prophylaxis by prevention of predisposing conditions, especially persistent vomiting, raised abdominal pressure, and excess acid, combined perhaps with local coating of the esophagus by a protective film, e. g., olive oil, might prevent or reverse the changes before final scarring occurs.

Occult Cancer of Breast. A. Dujovich and S. Srulijes. Rev. Asoc. méd. argent. **69:**394-396 (Nov. 15-30) 1955 (In Spanish) [Buenos Aires, Argentina].

Occult cancer of the breast starts with the occurrence of axillary metastases without either local symptoms or the presence of palpable nodules in the breast. Histological examination of the metastases surgically removed is the only procedure for the establishment of the diagnosis. If cancer is not found in the pleura, the lung, or in the gastrointestinal tract, a radical mastectomy by Halsted's technique followed by deep roentgen therapy is indicated. The subjects of this report were two women 66 and 61 years old respectively. The patients requested treatment because of loss of weight in presence of axillary tumors. The tumors had appeared in the left axilla one year prior to consultation in one case and several days prior to consultation in the second. One patient had only an extensive adenopathy, and the other patient had several small adenopathies. The breast in both cases was of normal aspect and there were no palpable lumps. Histological examination of the lymph nodes that were surgically removed showed metastatic carcinoma. Roentgen examination did not show cancer of the pleura, lung, or gastrointestinal structures. A radical mastectomy followed by postoperative deep roentgen therapy was planned. The first patient refused the operation. She did not report to the Hospital Department for one year. When she reported, she had an enormous tumor in the breast. The tumor was painful, infiltrating, and caused retraction of the nipple. There were several large lymph nodes in the axilla. Again the patient refused treatment. She died shortly after she reported to the hospital the second time. The second patient had radical mastectomy followed by administration of deep roentgen therapy. The histological diagnosis of the breast after surgical removal was epithelioma with globular, cubic, and cylindric cells. The patient was discharged from the hospital in satisfactory condition. She has been observed for three years after the operation and was still clinically cured at the time of writing. The author concludes that occult carcinoma of the breast corresponds to group 2 of Steinthal's and group 3 of Jungling's classification of cancer of the breast. The treatment is the same as that resorted to in any other type of cancer of the breast.

Aneurysms of the Aorta: A Clinicopathologic Study of 369 Necropsy Cases. P. Brindley and V. A. Stembridge. Am. J. Path. **32:**67-82 (Jan.-Feb.) 1956 [Ann Arbor, Mich.].

The data reported are based on autopsies performed in the pathology department of the University of Texas Medical Branch at Galveston from 1892 to 1953. During this 62-year period, 9,273 autopsies were recorded and in 369 cases one or more aneurysms of the aorta were demonstrated. The multiple lesions found in some aortas brought the total number of aneurysms studied to 412. The incidence of aortic aneurysms was about 4%. The majority were found in patients in the fifth, sixth, and seventh decades; however, aneurysms of the arch tended to occur in younger patients, whereas lesions of the abdominal aorta and multiple and dissecting aneurysms were found in older patients. Although aneurysms were more frequent in Negroes, dissecting aneurysms demonstrated an equal racial distribution and abdominal aneurysms were more commonly found in Caucasians. Syphilis was the etiological agent in over half the cases (54%). Aneurysms were most often saccular and usually involved only one anatomic segment of the aorta. Multiple and dissecting aneurysms were present in 11% and 12% of the cases respectively. An unexpected pathological finding was cardiac hypertrophy in over 80% of patients with a dissecting or abdominal aneurysm. The average duration of illness was two years for patients with syphilitic aneurysms and 27 months for those with arteriosclerotic aneurysms. Clinical signs and symptoms correlated well with the anatomic features of the aneurysms. While the immediate cause of death varied, rupture of the aneurysm was the most common single cause, being found in 39% of the cases. A comparative study of the first 100 cases, observed from 1892 to 1928, and the last 100 cases, observed during the period 1943 to 1953, indicated improvement in diagnostic acumen, better treatment, and a longer natural life span on the basis of the following trends: a decrease in the incidence of thoracic aortic aneurysms; an increase in aneurysms involving the abdominal aorta or both the abdominal and thoracic aorta; a decrease in syphilitic aneurysms; an increase of aortic aneurysms due to arteriosclerosis or cystic medial necrosis; an increase in the average age of patients with all types of aortic aneurysms; an increase in the age of patients with syphilitic aneurysms; and a decrease in the average age of patients with arteriosclerotic aneurysms.

RADIOLOGY

The Lower Esophageal Ring. R. Schatzki and J. E. Gary. Am. J. Roentgenol. **75:**246-261 (Feb.) 1956 [Springfield, Ill.].

The authors report on 11 men and 10 women with dysphagia caused by lower esophageal rings. The lower esophageal ring is a thin diaphragm-like constriction of the lower esophagus that is not infrequently found if the lower esophagus is distended with a barium mixture. This narrowing represents a thin annular portion of the wall of the esophagus that cannot be distended so well as the wall above and below the region. Occasionally this diaphragm is still clearly visible in the collapsed esophagus. Only 3 of the 21 patients were aged less than 50 years. The diameter of the opening in the ring varied considerably from patient to patient; the maximal diameter of the ring in the barium-distended esophagus ranged from 3 to 38 mm. With the exception of one patient, in whom there was a decrease of 3 mm. in the maximal diameter of the ring in eight years, the diameters of the rings remained constant for several years, including those in two patients who were followed up for five years. In some of the patients, the ring was located at the junction of the esophagus and a herniated portion of the stomach. This was proved at surgical intervention performed on one patient; in other patients the roentgenologic evidence, i. e., the shape of the pouch and the appearance of the mucosal pattern, seemed strong evidence of such a hernia. The ring must be differentiated from simple muscular contraction of the esophagus and from hiatal hernia with or without esophagitis. The cause of the ring is not known. It appears likely that some upward displacement of the intestinal tube into the chest is present in all patients with lower esophageal ring. The dysphagia in the patients was characterized by sporadic episodes of difficulty in swallowing solid food. These episodes seemed to depend primarily on the diameter of the maximally opened ring and to a lesser degree on the eating habits of the patients. In addition, the authors observed 64 persons in whom roentgenologic examination revealed a lower esophageal ring but who did not have dysphagia. All of the authors' patients in whom the diameter of the ring was less than 13 mm. had dysphagia and none with a diameter over 25 mm. had dysphagia. The consistent roentgenologic similarity between the rings in patients with dysphagia and in those without dysphagia suggest that the mechanism of the ring is the same. Although the nature of the ring remains problematic, the roentgenologic and clinical aspect in patients with dysphagia forms a definite entity that requires treatment. Satisfactory therapeutic results can usually be obtained by proper education of the patient to understand the necessity of eating slowly and of decreasing the size of the bolus. Most of the patients with a long follow-up still had occasional difficulties in swallowing, but less frequently and not severely. A very narrow ring may require plastic surgery.

Annular Pancreas in the Adult. G. D. Dodd and W. A. Nafis. Am. J. Roentgenol. **75:**333-342 (Feb.) 1956 [Springfield, Ill.].

Six cases of annular pancreas are described in adults, five men between the ages of 50 and 67 years and one 50-year-old woman. Symptoms ranging from vague, intermittent epigastric discomfort and belching or a feeling of fullness and nausea to severe epigastric pain and recurrent vomiting were observed in three patients. The three other patients were asymptomatic. The roentgen diagnosis of annular pancreas was confirmed by laparotomy in two patients and by autopsy in three patients. Although surgical intervention was not warranted in the sixth patient, the survey roentgenogram obtained was characteristic of a non-

obstructing annular pancreas in showing a constant deformity of the duodenal bulb and slight stasis above an eccentric narrowing of the descending limb. These findings were confirmed by a conventional study that showed a compressed but otherwise intact regional mucosa. Annular pancreas is a relatively common anomaly in which three phases may be observed clinically. The first phase is that of complete duodenal obstruction in the newborn in whom a plain erect roentgenogram of the abdomen will show the so-called double bubble sign that is representative of air-fluid levels in the dilated stomach and duodenum, and thus will indicate duodenal obstruction and the need for immediate surgical intervention. The second phase is that of obstruction of such minimal degree that the anomaly, which produces few or no symptoms, is usually an incidental finding at autopsy at any age. The third phase is that of chronic or acute duodenal obstruction occurring relatively late in life. Superimposed disease frequently initiates the obstructive symptoms in patients in the last group. Contrast studies of the stomach and the duodenum provide the only clinical method for establishing the diagnosis in adult patients. The characteristic roentgen findings are localized medial retraction of the second portion of the duodenum, thinning of the underlying mucosa, and eccentric narrowing of the lumen. Postbulbar ulceration and duodenal neoplasms provide the major differential problems, but careful analysis of the obstructive point should result in correct diagnosis in a high percentage of cases.

Leukaemia Following Radioiodine Treatment of Hyperthyroidism. E. E. Pochin, N. B. Myant and B. D. Corbett. Brit. J. Radiol. **29**:31-35 (Jan.) 1956 [London, England].

A woman, aged 41, had had nervousness, irritability, weakness, palpitations, and dyspnea on exertion for many years, with attacks of nausea and diarrhea. She had been losing weight despite a good appetite and had noticed trembling of her fingers. She had had three courses of treatment with thiouracil derivatives, improving considerably during each but relapsing on withdrawal of the drug. She was therefore treated with radioiodine, receiving a total of 6.8 mc. during a seven-week period terminating June 30, 1951. During the following year she gained weight, lost her tremor and eye signs, regained her energy, and became virtually free from symptoms of thyroid or other disease. In January, 1953, she started to feel increasingly breathless, with giddiness, headache, and paraesthesia in toes and fingers. A blood cell count in June, 1953, revealed 3,400 white blood cells per cubic millimeter, with numerous stem cells and other immature forms. The term stem cell is used for cells indistinguishable from lymphoblasts or myeloblasts but whose exact affinity is uncertain. A smear of sternal marrow was found to be highly cellular; 85% of cells were stem cells and 11% were early cells. The residual 4% of cells consisted of mature lymphocytes, plasma cells, and red blood cell precursors. She was treated with corticotropin and transfusion of four pints of packed red blood cells. Several months later, in October, 1953, she was readmitted with fever, tachycardia, and a pericardial effusion. She had leukemic deposits in the forearm and knees and widespread purpura. The blood showed 312,000 white blood cells per cubic millimeter. She died on Oct. 24. Autopsy revealed leukemic deposits in the pericardium, lung, liver, spleen, and kidney and in numerous lymph nodes. The authors feel that, unless the leukemia could have been initiated by irradiation within the thyroid or its capsule, it seems unlikely that the radioiodine treatment was relevant to the subsequent leukemia. One cannot exclude the possibility that radiation estimated at about 10 rep, or at less than 75 rep for cervical tissues or 100 rep for the liver, might have initiated leukemia, although a diagnostic barium meal with several minutes' screening could then equally be a cause of this condition. Radioiodine, as well as other forms of irradiation, may give rise to leukemia when it causes sufficiently massive irradiation of the body as a whole. Four cases have been reported of leukemia occurring after administration of radioiodine with other radiation treatment of thyroid carcinoma, in which condition very much higher doses are given than for hyperthyroidism. With the low doses used in the present case, it seems much more likely that the leukemia was unrelated to the previous irradiation. In women of 40 to 45, leukemia causes 25 deaths per million of population per year. One such death from leukemia should, therefore, arise purely by chance in 8,000 patients followed for five years after radioiodine treatment.

Microscopic Findings in Preoperatively Irradiated Carcinoma of the Breast. W. Grill. Arch. klin. Chir. **281**:101-108 (No. 2) 1955 (In German) [Berlin, Germany].

At the surgical clinic of the University of Marburg an der Lahn, Germany, exploratory excisions were performed in 20 women in whom carcinoma of the breast was suspected. Immediately after the diagnosis of carcinoma had been established and the exploratory wound had healed, roentgen irradiation was carried out from three fields, i. e., one medial-tangential, one lateral-tangential thoracic, and one supraclavicular field. Each field received a daily surface dose of 200 r, so that each field was given a total surface dose of 3,000 r in 15 irradiations. Ablation of the breast was carried out, as a rule four weeks later. In 5 of the 20 patients, microscopic examination of the operative specimen did not reveal a primary tumor or a metastasis after the irradiation. In a single case, in which the primary tumor had been removed completely by the exploratory excision, extensive metastases were observed in the axillary lymph nodes. Microscopic changes of the skin after the irradiation were similar to those generally observed after irradiation with high irradiation doses. Comparison of the microscopic findings in the specimen removed by exploratory excision with those in the removed breast always showed a definite irradiation effect that varied within certain limits. Considerably increased connective tissue with splitting of the tumor predominated, and there were severe regressive cell changes with atypical cells, hyperchromatosis of the nuclear wall, pyknosis, disintegration of the nucleus, and vacuolar degeneration of plasma. The regressive changes frequently were more pronounced in the metastases of the lymph nodes than in the primary tumor. Frequently the damage was so marked that the tumor cells could hardly be recognized as such. These findings prove the suitability of preoperative irradiation of carcinoma of the breast with respect to prevention of local recurrences and metastases.

PUBLIC HEALTH

Effects of Low-Level Radioactivity in the Columbia River. C. Henderson, G. G. Robeck and R. C. Palange. Pub. Health Rep. **71**:6-14 (Jan.) 1956 [Washington, D. C.].

The discharge of radioactive by-products of nuclear reactions into surface streams creates a problem in environmental sanitation in the atomic age. This report summarizes studies made by the Public Health Service to determine the effects of radioactive wastes on the Columbia River. Although many radioactive wastes and coolants are produced in the manufacture of plutonium at the Hanford plant, the only large effluent to enter the Columbia River directly results from the cooling of the nuclear reactors. The following are the major conclusions regarding radioactivity in the Columbia River derived from the studies carried out between 1951 and 1953: Low-level beta activity has had no adverse effect upon the numbers and species of aquatic organisms in the Columbia River. The radioactivity levels in plankton and attached algae are directly dependent upon levels in the river water. The radioactivity levels in aquatic animals vary with their metabolic rates (which in turn vary with water temperatures) and with the radioactivity levels of the materials upon which they feed. Migratory species in the Columbia River such as salmon, the adults of which do not feed in fresh waters, have low radioactivity levels at the same time that levels in resident species are high. While radioactive materials are found in all the body parts of fish, the activity levels are about 10 times higher in scales, bones, and internal organs than in the edible parts, such as muscle and skin. Since aquatic organisms concentrate specific radioisotopes such as phosphorus^{32} many thousand times above the levels in water, the use of these organisms for human or animal consumption presents a potential public health problem. However, to date the levels of radioactivity in the flesh of Columbia River fish are not dangerously high.

BOOK REVIEWS

Atlas of General Surgery. By Joseph R. Wilder, M.D., Assistant Professor of Surgery, New York Medical College, Flower and Fifth Avenue Hospitals, New York. Cloth. $13.50. Pp. 222, with 101 plates. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1955.

The author has drawn much of his material from standard textbooks and manuals of surgery. He states that many of the procedures outlined are in large part those of his teachers. This manual is to be used when a procedure may need review by the surgeon. Some of the techniques described are not preferred by all surgeons, but the principles are sound. The opening discussions, dealing with operating-room principles, are succinct. The subjects discussed include sterile technique, exposure and anatomy, care of tissues, hemostasis, selection of ligature material, knots, wound closure, drains, anesthesiologist-surgeon relationships, and operating time. The section on cardiac arrest is clear, with well-drawn illustrations of the technique suggested by the author. Seventy-three operative procedures are outlined. The author lists the important considerations for each operation. Line drawings of each operation, with appropriate legends, follow. No attempt is made to justify the method. This atlas should be most useful to the intern, resident, and the postgraduate student.

Glaucoma. Editor: Sir Stewart Duke-Elder. Symposium organized by Council for International Organizations of Medical Sciences established under joint auspices of UNESCO and WHO. Cloth. $7.50. Pp. 350, with 60 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., Toronto 2B, Canada, 1955.

This symposium consists of formal papers and discussions that followed dealing essentially with the newer findings and researches on glaucoma and its relationship to past and established knowledge. In the light of recent research, we must revise our thinking and our perspective. We must begin with a revision of terminology and the detailed microscopic and extraordinarily complex anatomy of the anterior chamber and posterior segment of the eye, and the optic nerve. Drainage channels in the intrascleral connections, channels between Schlemm's canal, and the episcleral, aqueous, and ciliary veins and ciliary plexus are all worthy of a closer look. We also learn that the trabecular tissue at the chamber angle has a complex physiology of its own and probably plays an important part in the regulation of intraocular pressure. This symposium not only presents the state of our current knowledge but also points out the problems to be solved. The photographs are excellent. All ophthalmologists should read this book in order to reorient their thinking on this problem.

The Shoulder and Environs. By James E. Bateman, M.D., F.R.C.S., Orthopaedic Consultant, Sunnybrook Hospital, Toronto, Canada. Drawings by Louise Gordon. Cloth. $16.25. Pp. 565, with 376 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1955.

The author of this book admirably achieves his objective in discussing disorders in and about the shoulder. The subject matter covered encompasses diseases of the shoulder, disorders of the neck as they are related to shoulder pain, and conditions causing pain that radiates to or from the shoulder. The material covered includes embryology, anatomy, physiology, pathology, and also the examination, clinical course, and treatment of the various diseases of the shoulder region. The chapter on differential diagnosis is excellent, and the tables of comparison increase the value of this section. Of special interest to the physician confronted with a compensation problem is the chapter on management and assessment of disability. The summary of treatment at the close of each chapter is particularly useful for quick reference. The book is easy to read, and the illustrations are superb. The quality of the paper and the type are excellent. The references at the end of each chapter are more than adequate. Though the operative procedures and the methods of therapy are not always conventional, they are challenging and rational. On the whole, the material is presented accurately and compares well with other books and monographs on this subject. This comprehensive book can be highly recommended to all who have an interest in diseases of the shoulder.

Atlas of Bronchial Lesions in Pulmonary Tuberculosis: A Clinical and Morbid-Anatomical Study. By C. Dijkstra, M.D., Medical Superintendent of Sanatorium 'De Klokkenberg,' Breda, The Netherlands. Translated from Dutch manuscript by Th. R. Heemskerk. Cloth. $11. Pp. 128, with 131 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Scheltema & Holkema N. V., Rokin 74-76, Amsterdam, The Netherlands, 1955.

This handsome monograph deals chiefly with the radiology and the gross microscopic lesions of bronchial tuberculosis. The first section discusses obstructive lesions associated with collapse and caseation; the second, obstructive lesions mostly associated with bronchiectasis; the third, residual lesions of obstructive infiltrations that are virtually inactive from the clinical point of view; the fourth, tuberculous bronchial lesions in the neighborhood of cavities and tuberculomas; and the fifth, bronchial changes in fibrotic and inactive lesions. In each section there is a series of case reports illustrated by roentgenograms, photographs of the gross surgical specimen, and photomicrographs of the pertinent bronchial or juxtabronchial tissues. The roentgenograms are well reproduced, and many of the gross tissue photographs are informative. It would be of some assistance to the reader if the legends for the specimens carried a notation indicating the approximate interval between the date of the accompanying roentgenogram and the date of operation. The cases are chosen from a series of over 500 resected specimens taken from patients treated at the Klokkenberg Sanatorium (Breda, Holland). The thoroughness of the investigations is indicated by a note in the preface dealing with examinations of sputum for tubercle bacilli: when direct examination of smears failed to reveal bacilli, cultures were grown every fortnight for several months or often years. This is indeed persistence. The text is clear. There is a brief bibliography and a closing discussion that should be of interest to phthisiologists, radiologists, and pathologists. In the next edition, pictures of whole lung slices made by the Jethro Gough technique would be an addition. There is an informative preface by Prof. W. Bronkhorst, of Utrecht.

Medical Department, United States Army, Surgery in World War II: Vascular Surgery. Edited by Daniel C. Elkin, M.D., and Michael E. DeBakey, M.D. Office of Surgeon General, Department of the Army. This volume was prepared by Historical Unit, Army Medical Service, under direction of Colonel Calvin H. Goddard, MC, AUS, and Helen Orr. Cloth. $4.25. Pp. 465, with 56 illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1955.

This volume on vascular surgery is among the first of many volumes to be published on the medical history of the U. S. Army in World War II. In the history of World War I the subject of vascular surgery was dismissed with a single paragraph, while neurosurgery, for example, was accorded 535 pages in one of the surgical volumes. Many technical advances in vascular surgery were made in the period between World Wars I and II. However, since vascular injuries are relatively infrequent in civil life, when World War II broke out there were few surgeons with extensive experience in vascular surgery. To supply competent specialized care for the large number of vascular injuries was a difficult problem that was solved in World War II by establishing three vascular centers to which surgeons experienced in this specialty were attached. Surgeons General James C. McGee and Norman T. Kirk are given credit for establishing these centers soon after the first casualties began to arrive in this country, and Brig. Gen. Fred W. Rankin, chief of the surgical service in the Surgeon General's Office, was largely responsible

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

for the success of this undertaking. He had the aid of Col. B. N. Carter and Col. Michael E. DeBakey. The first vascular centers were established at Ashford General Hospital, White Sulphur Springs, W. Va., and at Letterman General Hospital, San Francisco, on May 28, 1943. The former center was continued until June 30, 1946, and the latter was inactivated Dec. 23, 1943, when the patients on the vascular ward were transferred to Torney General Hospital, Palm Springs, Calif., and this one continued until June 12, 1944, when DeWitt General Hospital, Auburn, Calif., was designated as a hospital to which vascular patients should be sent. The third vascular center at Percy Jones General Hospital, Battle Creek, Mich., established June 12, 1944, was active only until Aug. 25 of that year, when Mayo General Hospital, Galesburg, Ill., became a vascular center and continued in operation until Oct. 17, 1946.

This volume was prepared by the historical unit of the Army Medical Service. It does not purport to be a complete record of casualties with vascular injuries in World War II, as data from such theaters of operations as China-Burma-India, Southwest Pacific, and Pacific Ocean areas and records from the North African, Mediterranean, and European theaters are far from complete. The book does give a reasonably complete accounting of complications that followed vascular injuries incurred in Army personnel in combat who were evacuated to the zone of interior. It includes also an account of peripheral vascular disorders in Army personnel during this war, with the exception of trenchfoot, immersion foot, and cold injuries, which will be discussed in a separate volume in the medical history series. In the 16 chapters on various phases of the care and treatment of casualties with vascular injuries are a number of halftone illustrations, some in color. There is an index. The editors have apparently accomplished their objective in an excellent manner.

Subacute Bacterial Endocarditis. By Andrew Kerr Jr., M.D., Assistant Professor of Medicine, Louisiana State University School of Medicine, New Orleans. Publication number 274, American Lecture Series, monograph in Bannerstone Division of American Lectures in Internal Medicine. Edited by Roscoe L. Pullen, A.B., M.D., F.A.C.P., Professor of Medicine, University of Missouri School of Medicine, Columbia. Cloth. $6.50. Pp. 343, with 7 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1955.

This is a well-documented, scholarly presentation of present knowledge of subacute bacterial endocarditis. The author not only has reviewed 800 original articles that are listed as references but has delved into the archives to find references to this condition in the writings of Lancisi, Morgagni, Corvisart, and others. The important contributions of Horder and Libman are given proper credit. There is an excellent chapter on etiology followed by chapters on the clinical findings and treatment. The importance of early treatment, even when an absolute diagnosis by blood culture has not been made, is emphasized. The value of the different antibiotics is weighed in the light of results reported in the literature, and it is concluded that only the bactericidal antibiotics are of real value. Therefore, although the organism obtained from the blood culture may show a high degree of sensitivity to such bacteriostatic agents as the sulfonamides or tetracycline, treatment with penicillin and streptomycin is still the therapy of choice. Since this disease is not common, most physicians should be happy to have this excellent reference book handy when called on to see a patient suspected of having subacute bacterial endocarditis.

Peripheral Vascular Disease. By A. J. Barnett, M.D., M.R.C.P., M.R.A.C.P., Assistant Director, Alfred Hospital Clinical Research Unit, Melbourne, Australia, and J. R. E. Fraser. Cloth. $9.50. Pp. 219, with 39 illustrations. Melbourne University Press, Carlton, N.3, Victoria, Australia; Cambridge University Press, 32 E. 57th St., New York 22, 1955.

This monograph attempts to present a practical approach to the problem of peripheral vascular disorders. It deals with the diseases, particularly those occurring in Australia, of the arteries and veins of the extremities. Disorders of the lymphatic channels are not considered. Technically the material is well presented and lucidly illustrated. The first section of the book consists of a chapter on a historical survey of the field, one on the physiology of the blood vessels, and one on methods of diagnosis of arterial insufficiency. A large part of the latter chapter is devoted to a description of laboratory procedures for the study of peripheral blood flow such as the venous occlusion plethysmographic method and calorimetry. Since these techniques have little or no clinical application, their emphasis in a small monograph on the practical aspects of peripheral vascular diseases appears pointless. In the second section the pathology of the various clinical entities is presented. Much of this section is devoted to pathological alterations in arteriosclerosis obliterans and the mechanism of intravascular clotting. In the final section, the clinical aspects of peripheral vascular disorders are discussed. A large number of case reports is presented to typify various phases in the clinical course of a disease entity, but for the most part they are too fragmentary to be helpful in this regard, and the reader is left with no clear-cut concept of any of the common disorders. In this section, two chapters are devoted to the treatment and prognosis of peripheral vascular diseases. A brief presentation of the pharmacology of vasodilator drugs is included. The plan of presenting the pathology, clinical characteristics, treatment, and prognosis of a vascular disorder in different portions of the book has little in its favor. This monograph compares unfavorably with most of the books already available in this field.

Recent Advances in Neurology and Neuropsychiatry. By Sir Russell Brain, Bt., D.M., P.R.C.P., Physician to London Hospital and Maida Vale Hospital for Nervous Diseases, London, and E. B. Strauss, M.A., D.M., D.Sc., Physician for Psychological Medicine, St. Bartholomew's Hospital. With assistance of Denis Hill, M.B., F.R.C.P., D.P.M., Douglas Northfield, M.S., F.R.C.S., and David Sutton, M.D., M.R.C.P., F.F.R. Sixth edition. Cloth. $7.50. Pp. 311, with 46 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, England, 1955.

The first edition of this work was published in 1929 and the fifth in 1947. This book is not a textbook per se but is rather an auxiliary textbook of applied neurology. It is clinically oriented, the authors choosing from the literature what they wish to elaborate on and coordinating the basic science as well as the clinical viewpoints. The present edition contains chapters not included in the preceding editions. Dr. Denis Hill has contributed a chapter on electroencephalography and Dr. David Sutton one or neuroradiology. The book considers the cerebral cortex, consciousness and unconsciousness, the cerebellum and its disorders, poliomyelitis, the demyelinating disorders, the intervertebral disc and spondylosis, the cerebral circulation, miscellaneous clinical and therapeutic advances, and finally electroencephalography, neuroradiology, and intracranial tumors.

This delightful book is well written and serves as a useful review. The authors have not, however, been as critical as they might have been. For instance, in the treatment of neurosyphilis, doses of penicillin are much smaller than those used by American neurologists, and some come below the critical level. It is also a little surprising to find that the "beaten silver" markings of the skull, even in adults, are considered to be of little diagnostic import or an indication of increased intracranial pressure. In the discussion of temporal lobe epilepsy, the use of sleep records is not attributed to Dr. Gibbs. In dealing with the problems of prefrontal leukotomy, the authors go out of their way to take issue with the American term "psychosurgery," labeling it as "barbarous." It is also surprising to find the positive assertion that most patients with myasthenia gravis should undergo thymectomy. The book is well illustrated by well-chosen and excellently reproduced photographs. The references are adequate, but no attempt has been made to include a complete bibliography of the literature. The references do not cite the title of the quoted article, merely the author's name, the journal, and the appropriate page and volume. This is the type of book that the neurologist thoroughly enjoys browsing through on a quiet evening. It tends to review for him some of the literature he has read in the past year, and, as the authors indicate, it will in no way suffice for the complete view of the field of neurology. To a practicing neurologist, the title is somewhat puzzling in that there is no section on psychiatry as such, and this is apparently due to a fundamental difference in concept between American and English neurologists.

QUERIES AND MINOR NOTES

PREVENTION OF TUBERCULOSIS AMONG STUDENT NURSES

TO THE EDITOR:—*Our school of nursing wants to set up a program for the prevention and early detection of tuberculosis for the student nurses. Please outline measures considered advisable. If BCG is considered advisable, please describe the mode of administration.*

M.D., Maryland.

ANSWER.—The best method devised to date for the prevention and early detection of tuberculosis among students of nursing consists of testing all entering students with tuberculin. Those reacting have prompt examinations, including x-ray film inspection of the chest. These examinations should always be complete, as 10 to 15% of clinical lesions develop extrathoracically. If no clinical disease is found among the reactors on entrance, complete examination, including x-ray films of the chest, should be made at least semiannually. Those students in whom lesions are destined to evolve will usually be found before symptoms appear and before their conditions are contagious. Moreover, most of them can be treated successfully at that time. One must not overlook the possibility of acute forms of tuberculosis, such as meningitis, miliary disease, and pleurisy with effusion, among those who react to tuberculin on entrance. Therefore, all such students should be instructed to report promptly when any illness occurs, although it may seem minor to them. Early diagnosis is important since antimicrobial drugs are now available. Those students who do not react to tuberculin on entrance should have the test administered at least semiannually, so that if infection does occur it will be detected promptly. Converters should be completely examined, and, if no clinical disease is found, semiannual examinations are in order just as for those who are reactors on entrance. Considerable enthusiasm is being manifested for administering antimicrobial drugs as soon as possible after students convert from negative to positive tuberculin reactors. At that time, lesions are usually microscopic and vascular and drugs in the blood stream may be expected to come in contact with all tubercle bacilli. Whether they are capable of destroying all organisms has not been determined, but considerable evidence has accrued to show that the bacilli are so suppressed that acute forms of the disease like meningitis and generalized miliary tuberculosis are not likely to develop. Schools of nursing that have adopted this preventive program have reduced the number who convert from negative to positive tuberculin reactions to an exceedingly low level. Students must be protected against patients who enter hospitals for one condition and have unsuspected coexisting contagious tuberculosis. This is done most effectively by examining all patients on admission to hospitals for tuberculosis. Hospital personnel members have preemployment examinations and are checked at least semiannually during employment. In such institutions, barring errors in diagnosis, students rarely become infected while on duty. For those who must care for tuberculous patients, even for a brief time after diagnoses are made, effective rigid contagious disease technique is available. If students are sent on affiliations to other hospitals, there should be assurance that those institutions have patient admission and personnel members' examinations. If such hospitals have tuberculosis services, rigid contagious disease technique must be employed to protect affiliate nurses as well as others. Inasmuch as an attack of tuberculosis, either mild or severe, does not produce dependable immunity, there is no premise for attempts to produce immunity artificially by any one of the several agents now available in this country and abroad, including BCG. The original bacille Calmette Guérin (BCG) was a bovine type of tubercle bacillus, isolated in 1902. Its virulence was reduced by Calmette and Guérin, who gave it their names in 1921. At that time, it consisted of a single bacterial form. However, mutation apparently has occurred in the various cultures, so that those recently examined contain multiple bacterial forms and no two are alike. Some of these mutants are quite invasive for animal tissue and apparently are responsible for the large number of clinical abscesses and ulcers, as well as lymphadenitis, that have been reported in persons who have received BCG. Soon after BCG administration, numerous tuberculous lesions have been reported in other locations, such as the eyes, bones, and lungs. There are now five well-documented cases of deaths resulting from BCG. Bacilli from others who have died are now being carefully studied.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

HYPOTENSION

TO THE EDITOR:—*I would like to know how to manage hypotension in patients who really have symptoms and have systolic blood pressures of 90 mm. Hg or less. Physical examination and laboratory work do not reveal any positive findings. The amphetamine group of drugs fails to produce significant results. Please expound on the theories in such cases.*

M.D., New York.

ANSWER.—There is no wholly satisfactory treatment for true chronic hypotension. The condition has been thought to be due to an inadequate sympathetic vasomotor supply and occasionally to be associated with a variety of spinal cord diseases. The proof for these statements leaves much to be desired. Probably the commonest cause of alternating hypotension and normotension is chronic debility with the loss of the muscle tone. Hypoadrenia is a less common cause. Cortical hormone therapy has not been given an adequate trial in chronic hypotension and is worth a try. Another possibility worthy of trial is administration of 1% saline solution as drinking water. A "head-up" bed may also be tried.

INFECTIONS DUE TO MIMA ORGANISMS

TO THE EDITOR:—*I would like information about a gram-negative organism named Mima polymorpha that apparently belongs in the family Parvobacteriaceae. Has this organism's pathogenicity been limited to causing vaginitis and conjunctivitis?*

M.D., Connecticut.

ANSWER.—The tribe Mimeae consists of three genera—Mima, Herrella, and Colloides. Sorrell and White (*Am J. Clin. Path.* **23**:134, 1953) reported a fatal case of acute bacterial endocarditis in a human being caused by a variant of the genus Herrella in which the organism was isolated from the blood stream. References are also given in the same article to the isolation of pure cultures of Mima polymorpha from the cerebrospinal fluid in cases of meningitis and from the blood in cases of fulminating septicemia and subacute bacterial endocarditis. Terramycin appears to be effective in treating infections due to Mima organisms.

CROSSED CYLINDER IN REFRACTION

TO THE EDITOR:—*After using a crossed cylinder for a number of years, I have decided that the value of this instrument in checking the strength of the cylinder is questionable. Please let me know the opinion of others.*

Charles H. Henderson, M.D., Norton, Va.

ANSWER.—A crossed cylinder offers a convenient method of allowing the patient to compare an image with more or less cylinder added. If the sphere is such as not to fog the patient, it is a most accurate method. Many refractionists look upon it as one of the final steps in refinement of a refraction.

LARGE FAT DEPOSITS ON LEGS

To the Editor:—*A patient complains of extremely large fat deposits on both calves that have been gradually progressive and unaccompanied by other symptoms. The patient is about 6 ft. (182.88 cm.) tall, large-boned, and plump. The growth of the calves exceeds that of her thighs. The ankles are trim. The calves are so large as to interfere with normal gait (necessitating a slight out-swinging of each leg in passing the other but with no true gait deformity). The patient appears otherwise normal physically and mentally. The clitoris is normal-sized. 17-Ketosteroid excretion and thyroid functions are normal. Could you suggest a diagnosis and treatment?*

M.D., California.

Answer.—The inquiry does not give the age of the patient or how long the condition has existed; however, as size seems to be the only complaint, most probably this represents a type of muscle dystrophy. That there is no swelling of ankles precludes any vascular or lymphatic disease. The absence of pain rules out adiposis dolorosa (Dercum's disease) in which fatty deposits cause localized swelling and favorite sites are the ankles, which were spared in this case. Of the muscular dystrophies, pseudohypertrophic muscular dystrophy appears early in childhood and almost exclusively in males (most appear at 2 to 6 years of age, but delayed onset up to 20 years of age is noted). This type of dystrophy involves a large part of somatic musculature, and, in spite of the apparent athletic appearance and firm (rubbery) feel, these muscles are weak. Hypertrophy of muscle occurs in myxedema, other endocrine diseases, periodic paralysis, and myotonia congenita (Thomsen's disease), but each of these diseases has associated signs and symptoms not mentioned in the inquiry. According to Alpers, true hypertrophy, or hypertrophia musculorum vera, occurs in extremely rare cases in infants, giving the infant the appearance of Hercules, with large, well-proportioned, but weak, muscles. Muscles in this condition are firm but fatigue easily. In "Diseases of Muscle" (New York, Paul B. Hoeber, Inc., 1953), Adams, Denny-Brown, and Pearson state, "There exists in medical literature isolated observations of true hypertrophy of muscles without accompanying atrophy or other signs of dystrophy." The strength is usually increased, and pathologists agree that the only uniform change is in the enlargement of the muscle fibers. This case might be one of the latter group, although any case of muscular hypertrophy must be studied carefully to rule out myopathic disease. Biopsy must be seriously considered in this case.

FIBROCYSTIC DISEASE OF PANCREAS

To the Editor:—*A patient has two children, one being normal as far as is known, while the second child suffers from fibrocystic disease. The patient is anxious to know the possibility of her future offspring suffering from this condition.*

M.D., Pennsylvania.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Fibrocystic disease of the pancreas is considered a familial disease, the hereditary transmission being through recessive genes. When both parents have such recessive genes the chances of their offspring having the disease are about one in four. If such parents have one child with fibrocystic disease, then the chances of each successive child being born with the disease are one in four. It is not uncommon to see three or four successive children in a family with the disease, and families have been reported with seven or more cases. Parents of a child that has fibrocystic disease should be told that the chances of having a successive child with the disease are not more than one in four.

Answer.—Fibrocystic disease is said to occur once in every 1,000 to 10,000 in the general population. In families in which the disease has appeared, it can be expected to reappear in one out of every four subsequent children, irrespective of the number of previously affected children. A comprehensive review of the subject was made by Bodian (Fibrocystic Disease of the Pancreas: A Congenital Disorder of Mucus Production—Mucosis, New York, Grune & Stratton, Inc., 1953).

TOILET ROOMS

To the Editor:—*I would like information on the removal of odors from the air of toilet rooms. Is there a substance better than activated charcoal?*

G. J. Bloemendall, M.D., Ipswich, S. D.

Answer.—The clean, well-ventilated toilet room is not associated with persistent offensive odors. Temporary odors are obvious. To combat these odors, masking agents are acceptable, but they do not destroy odor; they merely superimpose a less disturbing odor. At present an acceptable masking agent is found in a commercial preparation, Alamask, supplied by the Rhodea Company of New York City. Sprays of this chemical will combat odors in toilet room atmospheres. This chemical has been found in use mainly in industrial establishments within the offensive trades, where the provided sprays are continuous. It is not known whether this compound is available in propelled, bomb-type units suitable for household use, but this would be desirable. Time-honored masking agents such as pine, sassafras, or creosote oil are not objectionable, but the persistence of the odor of these masking agents is as disturbing to some individuals as the fleeting odors of alvine materials. Activated charcoal is a good odor-absorbing medium, but its application is scarcely practical around most toilet rooms.

FLIGHT AFTER PNEUMONECTOMY

To the Editor:—*How high may a person fly in commercial airplanes after a complete right pneumonectomy?*

John D. Wilson, M.D., Evansville, Ind.

Answer.—A person with a complete one-sided pneumonectomy, provided there are no other complications like extreme overextension or residual pathology of the remaining lung, may be permitted to fly in commercial airplanes as high as 5,000 ft., equivalent to an atmospheric pressure of 12.23 lb. per square inch or 632 mm. Hg. In airplanes equipped with pressurized cabins, as most commercial airplanes are, the patient may fly at any altitude, provided the cabin pressure is maintained at the above-mentioned value or higher.

PRIAPISM AND ANTIHISTAMINES

To the Editor:—*In the past few weeks, I have seen two children with priapism, one 3 years old and the other 5½ years old. Both have nasal allergy. Here in south Texas we are in ragweed season. Both of these children have been receiving antihistamines. Has priapism ever been described as an effect of antihistamines?* *M.D., Texas.*

Answer.—It is not surprising that antihistamines may cause priapism. The antihistamines may cause a variety of autonomic and central nervous system disturbances, such as mental irritability, insomnia, tachycardia, tremors, muscle excitability and spasm, increased urinary frequency, difficulty in urination, and decreased libido. Priapism could also be a result of such nervous system disturbances. It would be expected, however, to be accompanied by other evidences of irritability of the central or autonomic nervous systems.

ACNE

To the Editor:—*What is the status of diethylstilbestrol therapy for severe acne during adolescence? Two patients, aged 14 and 16, have been under my care and that of a skin specialist without much improvement. Please state dosage and complications from this therapy, if any.* *M.D., Florida.*

Answer.—Treatment with estrogenic substances is usually effective in those cases of acne in which there is exacerbation just prior to the menses. Not all patients are benefited, but the majority are. Generally small doses are effective (0.1 mg. of diethylstilbestrol daily for 10 days prior to onset of menses), though in some cases the dosage must be increased or a natural estrogenic substance must be employed, particularly if the preparation produces cramps, nausea, vomiting, fever, or premenstrual tension.

REHABILITATION

To the Editor:—*A middle-aged patient is left with some ataxia of forearm, hand, and foot following a brain tumor operation. What literature or advice may I procure to aid in giving him the proper exercises?*

Allan L. Richardson, M.D., Naubinway, Mich.

Answer.—Since coordination involves a multiplicity of neurophysiological mechanisms, incoordination may result from injury or disease of any of its components. Attempts at overcoming incoordination or ataxia depend on recognition of the underlying mechanism damaged and an appreciation of its role in coordination. Treatment is directed at correcting this factor, if it is at all possible. If we are to assume that the disability in this case is primarily an ataxia, as commonly encountered in cerebellar dysfunctions, without weakness, sensory abnormality, or spontaneous involuntary movements, the treatment potentials are limited. The treatment consists of a prolonged process of repetitive exercises in order to increase the residual skills. Frenkel's exercises often are of limited but definite value.

References

Tidy, N. M.: Massage and Remedial Exercises in Medical and Surgical Conditions, ed. 9, Baltimore, Williams & Wilkins Company, 1952.

Krusen, F. H.: Physical Medicine and Rehabilitation for the Clinician, Philadelphia, W. B. Saunders Company, 1951.

Gordon, E. E.: Multiple Sclerosis, Application of Rehabilitation Techniques, New York, National Multiple Sclerosis Society, 1951.

PAIN OVER GALLBLADDER FOLLOWING ACCIDENT

To the Editor:—*A patient who was in an automobile accident sustained no injury, but he complained of pain in the right upper quadrant following this accident. X-ray revealed the man had cholelithiasis. He subsequently had a cholecystectomy, with complete alleviation of symptoms. The question has come up whether such an accident might jar heretofore firmly well-fixed stones down into the cystic duct and produce trouble.* *M.D., Pennsylvania.*

Answer.—It is entirely possible that trauma to the abdomen could dislodge gallstones in such a way that they might pass into the cystic duct and produce biliary colic. It is also possible that a gallbladder distended with stones would be more easily injured by blunt trauma to the abdomen than would a normal gallbladder. A serosal tear could produce tenderness and pain in the region of the gallbladder.

CECOTOMY

To the Editor:—*Would cecotomy to differentiate a cecal carcinoma from an inflammatory mass due to diverticulitis be an accepted procedure? Should the opening be closed or exteriorized? If closed, would you insert a drain?*

M.D., New York.

Answer.—Cecotomy may be an accepted procedure to differentiate cecal carcinoma from an inflammatory mass due to diverticulitis. However, it is not always possible clinically, even with the aid of frozen-section tissue examination, to determine the exact diagnosis because of the associated edema secondary to the inflammatory process. In most instances, therefore, it is more logical to do a hemicolectomy on the right, with an ileotransverse colostomy. If the inflammatory disease is limited and the diagnostic efforts are considered adequate, the opening in the cecum may be closed rather than exteriorized. No drainage is indicated.

FITTING SHOES WITH X-RAY MACHINES

To the Editor:—*I would like any information available on the use of x-ray machines for visual fitting of shoes, particularly regarding any health hazards connected with this practice.*

J. Karefa-Smart, M.D., Nigeria, Africa.

Answer.—It should be possible, under ordinary circumstances, to properly fit shoes without the use of x-ray visualization of the foot within the shoe. Although it is doubtful that injury due to x-rays will result to the foot of the adult person being fitted, physicians have expressed some concern in the case of children whose epiphyses have not yet closed. Although this hazard has not been clearly demonstrated in the case of shoe-fitting machines, individuals, particularly children, should be cautioned against repeated exposures to the feet as might occur, for example, in shopping from store to store whereby numerous visualizations of the feet by x-ray were carried out. Devices should be adequately shielded so as to minimize the possibility of injury from x-rays to shoe salesmen operating such machines.

ENDOMETRIOSIS OF THE PLEURA

To the Editor:—*How often have cases of endometriosis included pulmonary lesions?* *M.D., New York.*

Answer.—The first case of endometriosis of the pleura was reported by Nicholson (*Thorax* **6**:75 [March] 1951). This case was reported from the point of view of the thoracic lesion. The same case was reported from the gynecologic aspect by Barnes (*J. Obst. & Gynaec. Brit. Emp.* **60**:823 [Dec.] 1953). In this case endometriosis of the right ovary was discovered at laparotomy 18 months after the operation for decortication of the affected lung. Barnes says: "The occurrence of endometriosis in the pleura without apparent involvement of the rest of the lung and with no apparent lesion elsewhere except in the ovaries would appear to be explicable only on the basis of metaplasia or heteroplasia occurring in the pleura itself, which it must be remembered is developed originally from the coelomic cavity and this has a common origin with the peritoneum."

HEADACHE IN YOUNG GIRL

To the Editor:—*An 8-year-old slightly overweight girl has severe periodic headaches at intervals of about two months, or she may have two or three attacks within a few days. These headaches come on suddenly without warning, cause excruciating pain over the vertex of the skull, and cause extreme tenderness of scalp over vertex. After the child vomits two or three times the headache disappears. Blood studies, urinalysis, x-rays of the skull, and spinal fluid studies have all been normal. Please discuss probable cause and treatment.*

Harry E. Schaefer, M.D., Manitowoc, Wis.

Answer.—Unless the condition has existed for some time the roentgenograms of the skull should be repeated, as vomiting may occur in the absence of signs of intracranial pressure in cerebellar, fourth ventricle, and medullar tumors. Otherwise, recurrent headaches at variable intervals would indicate migraine. The pain is frequently associated with tenderness of the scalp. Vomiting gives relief, which is thought to be due to vagal stimulation. A test of 1 mg. of ergotamine tartrate in one-half glass of water immediately at onset of the attack, and repeated one-half hour later if necessary, should control the pain. Treatment would be to avoid strain or overwork and correct errors of refraction, sinus infection, and infected teeth, if present. The diet should also be checked for allergic factors (Glaser, J.: *A. M. A. Am. J. Dis. Child.* **88**:92 [July] 1954).

REMOVAL OF CALCULUS IN PAROTID DUCT

To the Editor:—*A middle-aged white man had a small calculus impacted in the distal end of the parotid duct. The ampulla was grasped with a hemostat and light traction applied. The distal end of the duct, including the calculus, was then snipped off with a fine pair of scissors. No bleeding occurred, and no sutures were employed. No complications have developed, and the patient has been relieved by the operation. Is this a sound, recognized procedure?* *M.D., Michigan.*

Answer.—The procedure described seems to have been satisfactory in this particular case. The technique used necessarily sacrifices mucous membrane and introduces the possibility of obstruction to the parotid duct by scar and stricture of the duct. A safer procedure would be a linear incision that "fish mouthed" the orifice of the duct and permitted dislodging the calculus with the point of a no. 11 Bard-Parker blade.

TETANUS IMMUNIZATION

To the Editor:—*In the Queries and Minor Notes section of* The Journal, *Dec. 24, 1955, page 1699, is a question regarding the choice of alum-precipitated versus fluid tetanus toxoid for immunization of adults, particularly with reference to booster immunization. The question and the answer both are misleading in some respects. The inquirer "was not sure whether it (alum-precipitated toxoid) or plain tetanus toxoid should be used in adults." The fact is that both fluid and precipitated tetanus toxoids have been used in millions of adults with virtually no reactions. The story of a patient receiving a booster shot of alum-precipitated tetanus toxoid followed in a few hours by a chill and high fever is so unusual that one wonders whether the agent injected might have been diphtheria-tetanus toxoids (pediatric type). Such a reaction, due to tetanus toxoid alone, will hardly be seen more than once or twice in a lifetime of practice. The statement in the answer that toxoids were formerly not advised for people over 10 years of age was true only for diphtheria toxoid and never for tetanus toxoid. More than 20 million adult Americans received tetanus toxoid during and after World War II, not to mention the millions of military personnel in Canada, Great Britain, France, and elsewhere who were similarly inoculated. Moreover, since 1949, all American military personnel have received alum-precipitated toxoid and reactions have been practically nil. In a special study some 25,000 men injected with alum-precipitated tetanus toxoid at an Army training camp a few years ago were watched for reactions, and not one man reported to the dispensary because of a reaction to the toxoid. Incidentally, it should be noted that the long history of absence of reactions to tetanus toxoid is quite unrelated to the relatively recent chemical refinement of this product. The contrary, however, is true for diphtheria toxoid, where refinement of the product reduces the number of reactions markedly.*

It was suggested that the Moloney test might be utilized before the injecting of tetanus toxoid. This test, which is a classic procedure for screening individuals who are sensitive to diphtheria toxoid, really has no application in routine tetanus immunization. The use of a sensitivity test such as the Moloney test has never been standardized for tetanus toxoid, and its interpretation therefore in such a situation would be difficult. Moreover, in an emergency the answer to a Moloney test would be obtained too late. If there actually were an individual who gave a history of a febrile reaction to tetanus toxoid and who required a routine booster injection, the logical procedure would be to give a small test dose (0.1 cc.) followed in 12 to 18 hours by as much of the remainder of the dose as the patient's reaction to the test justified. Similarly, if he required an emergency booster, the best procedure would be to inject 0.1 cc. of toxoid immediately and give more 12 hours later if the small dose caused no reaction. In any case, whether a test dose or a full dose is given, tetanus toxoid should be administered without delay when it is indicated.

The medical services of the three armed forces do not, as the answer stated, administer three doses of tetanus toxoid "at intervals of from one to two months." The official regulations, in effect for several years, state: "The second injection (of tetanus toxoid) will be given 1 to 2 months after the first and the third, approximately 12 months after the first." The long interval between second and third doses is immunologically very important. Regarding the question of whether to give fluid or alum-precipitated toxoid as an emergency booster, whereas both have been used effectively in thousands of patients with contaminated wounds, there is some theoretical reason to favor fluid toxoid. Some investigators have claimed that the response to a booster dose of fluid toxoid appears about a day sooner than with precipitated toxoid. Where only alum-precipitated toxoid is at hand, it should be used without hesitation and with complete confidence in its great effectiveness.

Geoffrey Edsall, M.D.
Director, Commission on Immunization
Walter Reed Army Institute of Research
Washington 12, D. C.

PARASITES IN PIGEONS

To the Editor:—*In the Queries and Minor Notes section in* The Journal, *Jan. 28, 1956, page 341, is an inquiry regarding the possibility of pigeons outside of a child's room shedding parasites that might cause a skin rash. Since this type of incident may occur more often than we realize, my two experiences may be of interest. Three years ago an anxious parent from a nearby rural community asked for help to rid her children's bedroom of a small insect that seemed responsible for a rash on them. I asked for insect specimens, and they were identified at the Army Biological Research Center as Dermanyssus avium et gallinae, which was described as a mite principally infesting pigeons and chickens. Under the eaves of the house just above the children's bedroom window were a series of pigeon nests. It was summer and the windows were left open, but, despite screens, the insects came in the house in large numbers. A roofing company screened off the roosting places under the eaves, and the family used a chlorophenothane aerosol bomb to kill the mites that were in the house. With the departure of the pigeons, the mites disappeared too. I am told that several other families have rid their houses of this annoying insect by similar procedures. The other case was similar in background, although the house was old and in a poorer neighborhood. In this case the mite was identified as the tropical rat mite, Liponyssus bacoti. There was a dirt space beneath part of this house in addition to a dirt cellar. Various pipes from the cellar passed upward into the house through this area. The holes in the floor through which the pipes passed were not closed. A rat extermination program was carried out; the space beneath the house was closed off as completely as possible, and tight collars were placed around the pipes to seal this passage. In addition, chlorophenothane was used liberally on the first floor and on the pipes where they came through the floor. The nuisance was promptly eliminated. Except that I might now advise malathion instead of chlorophenothane as an insecticide of somewhat lower hazard to man and wider range of effectiveness, the above approach is the solution to these problems. These pigeon or fowl mites are reported by Stitt, Clough, and Clough (Practical Bacteriology, Haematology and Animal Parasitology, ed. 9, New York, Blakiston Company, 1938) as producing in man ". . . a sort of eczema on the backs of the hands and forearms, similar to scabies, . . ." and the rat mite is said to have been incriminated as a carrier of endemic typhus; the authors further state that these mites "produce a dermatitis." These possibilities should be kept in mind, especially in rural areas, where chickens, pigeons, and rats are more apt to be found.*

Forbes H. Burgess, M.D.
Deputy State Health Officer
State Department of Health
Frederick, Md.

ECZEMA AT ONSET OF MENSTRUATION

To the Editor:—*In answer to a query on eczema in* The Journal, *Jan. 28, 1956, page 341, both consultants implied that the eczema in the patient discussed was part of the premenstrual syndrome complex and that the patient might respond to accepted methods of treatment for premenstrual tension, i. e., with progesterone, ammonium chloride, or androgens, plus supplemental therapy with reserpine or chlorpromazine, if necessary. I am afraid that the patient in question may be sorely disappointed with the therapy offered. It has been my experience that patients with eczema related to the menstrual period do not respond to the regimen outlined above but do respond to cyclic adrenocorticotropin therapy, given intramuscularly on the 20th, 23rd, and 26th days of the cycle, or to the use of small doses of cortisone-like hormones, such as prednisone, 2.5 mg. twice a day, administered orally throughout the cycle or during the last half of the cycle.*

Robert B. Greenblatt, M.D.
Department of Endocrinology
Medical College of Georgia
Augusta, Ga.